Paul Schulwitz

Access DB# 110471

SEARCH REQUEST FORM

RECEIVED
DEC 15 2003

Scientific and Technical Information Center

Requester's Full Name: Rebecca Lobo Examiner #: 89826 Date: 12/15/03
Art Unit: 1614 Phone Number 308-4724 Serial Number: 09/843132
Mail Box and Bldg/Room Location: Cm1 230 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): John McKeown

Earliest Priority Filing Date: 12/23/98

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please provide structures for
irinotecan
celecoxib
prevent, reduce recurrence
& search each to treat neoplasm or cancer

Thanks
Rebecca

Rush Search
Approved
TR Page

STAFF USE ONLY

Searcher: _____
Searcher Phone #: _____
Searcher Location: _____
Date Searcher Picked Up: 12/16
Date Completed: 12/16
Searcher Prep & Review Time: 15
Clerical Prep Time: _____
Online Time: _____
Total Search Time: 15

Type of Search

NA Sequence (#): _____
AA Sequence (#): _____
Structure (#): 2
Bibliographic: _____
Litigation: _____
Fulltext: _____
Patent Family: _____
Other: _____

Vendors and cost where applicable

STN: 36.12
Dialog: _____
Questel/Orbit: _____
Dr. Link: _____
Lexis/Nexis: _____
Sequence Systems: _____
WWW/Internet: _____
Other (specify): _____

STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 110471

TO:	From:
Rebecca Cook Location: CM-1/2B07/2D01 Art Unit: 1614 Tuesday, December 16, 2003 Case Serial Number: 09/843132	Paul Schulwitz Location: Biotech-Chem Library CM1-6B06 Phone: 305-1954 paul.schulwitz@uspto.gov

Search Notes

Examiner Cook,

See attached results.

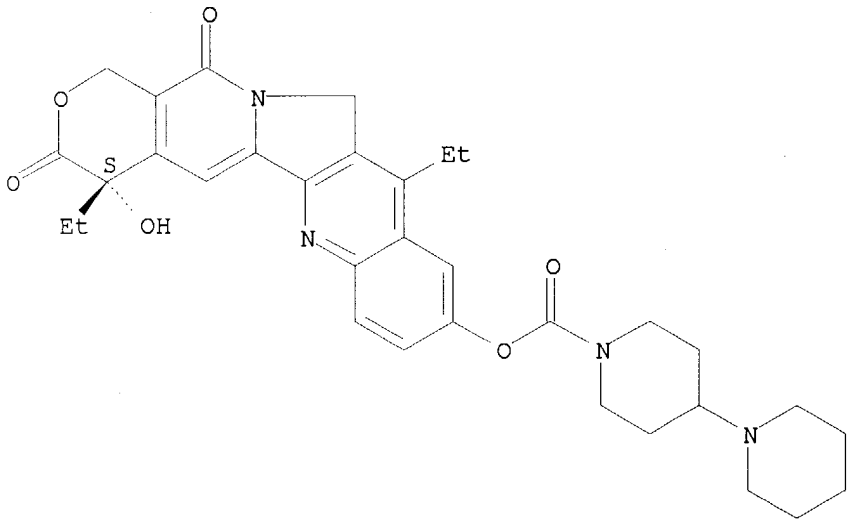
If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

Paul Schulwitz
Technical Information Specialist
STIC Biotech/Chem Library
(703)305-1954

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 97682-44-5 REGISTRY
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline, [1,4'-bipiperidine]-1'-carboxylic acid deriv.
CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, (S)-
OTHER NAMES:
CN (+)-Irinotecan
CN Camptosar
CN **Irinotecan**
FS STEREOSEARCH
MF C33 H38 N4 O6
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

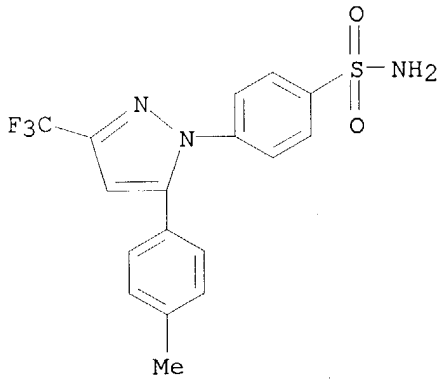
Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

761 REFERENCES IN FILE CA (1907 TO DATE)
19 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
770 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 169590-42-5 REGISTRY
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-[5-(4-Methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide
CN Celebrex
CN **Celecoxib**
CN Celocoxib
CN SC 58635
CN YM 177
FS 3D CONCORD
DR 184007-95-2, 194044-54-7
MF C17 H14 F3 N3 O2 S
CI COM
SR US Adopted Names Council
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
714 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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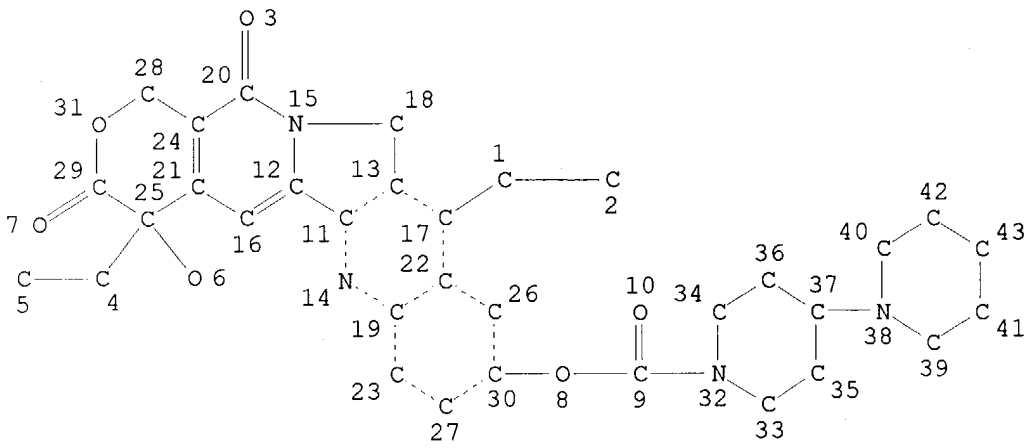
L2 STR



Irinotecan

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 43

AND

STEREO ATTRIBUTES: NONE
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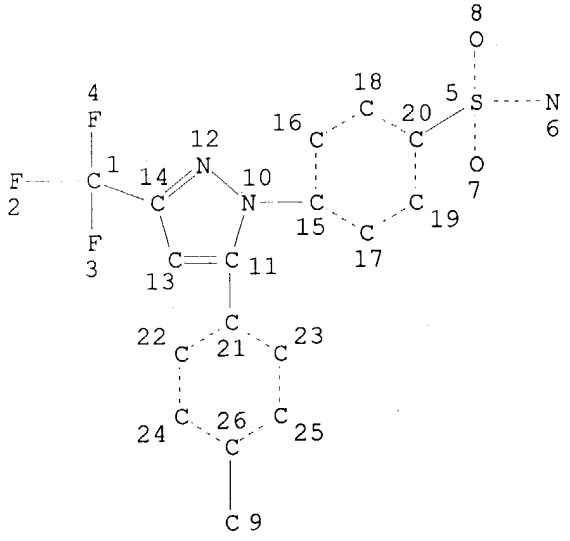
L5 STR



celecoxib

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE

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L6           26 SEA FILE=REGISTRY FAM FUL L5
L7         1080 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3(L)(BAC OR DMA OR PAC OR
                PKT OR THU)/RL
L8          665 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6(L)(BAC OR DMA OR PAC OR
                PKT OR THU)/RL
L10      166201 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTITUMOR AGENTS+OLD/CT
L11         955 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L10
L12         137 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 AND L10
L13           9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND L12
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9 references with Both irinotecan and Celecoxib as antineoplastics

=> d l13 ibib ab hitind hitstr 1-9

L13 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:511153 HCAPLUS
DOCUMENT NUMBER: 139:69281
TITLE: Preparation of alkynyl thienopyrimidines as protein tyrosine kinase inhibitors useful against cancer and other disorders
INVENTOR(S): Caferro, Thomas R.; Chamberlain, Stanley Dawes; Donaldson, Kelly Horne; Harris, Philip Anthony; Gaul, Michael David; Uehling, David Edward; Vanderwall, Dana Edward
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 240 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053446	A1	20030703	WO 2002-US39872	20021213

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-342207P P 20011219
OTHER SOURCE(S): MARPAT 139:69281

AB The present invention relates to alkynyl thienopyrimidines (shown as I; variables defined below; e.g. N-(2-benzyl-1H-benzimidazol-5-yl)-6-ethynylthieno[3,2-d]pyrimidin-4-amine), salts thereof, as well as use and prepn. of the same. These compds. are inhibitors of various protein tyrosine kinases (PTKs) of the ErbB family and consequently are useful in

the treatment of disorders mediated by aberrant activity of such kinases. Semiquant. pIC50 values for inhibition of ErbB-2 tyrosine kinase and IC50 values for cytotoxicity for HFF as a representative human normal cell line are reported for 11 examples of I. For I: one of A1 and A2 is S and the other is CH; R1 is H or -(CR11R11)n-R5; R2 is H or OC1-6alkyl; R3 = aryl (un)substituted with .gtoreq.1 halo, alkynyl, -CF3, -(CH2)nOR4, -(CH2)nSR4, -NO2, C1-6alkyl, -CN, -SO2R9, -(CH2)naryl and -(CH2)nNR9R10, and heteroaryl (un)substituted with .gtoreq.1 halo, alkynyl, -CF3, -(CH2)nOR4, -(CH2)nSR4, -NO2, C1-6alkyl, -CN, -SO2R9, -(CH2)naryl and -(CH2)nNR9R10; n = 0-6; addnl. details are given in the claims. Although the methods of prepn. are not claimed, .apprx.120 example prepns. of I are included.

IC ICM A61K031-519
ICS C07D495-04; A61P035-00; A61P017-06

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT **Antitumor agents**
Cytotoxic agents
Cytotoxicity
Drug delivery systems
Human
Neoplasm
Psoriasis
(prepn. of alkynyl thienopyrimidines as protein tyrosine kinase inhibitors useful against cancer and other disorders)

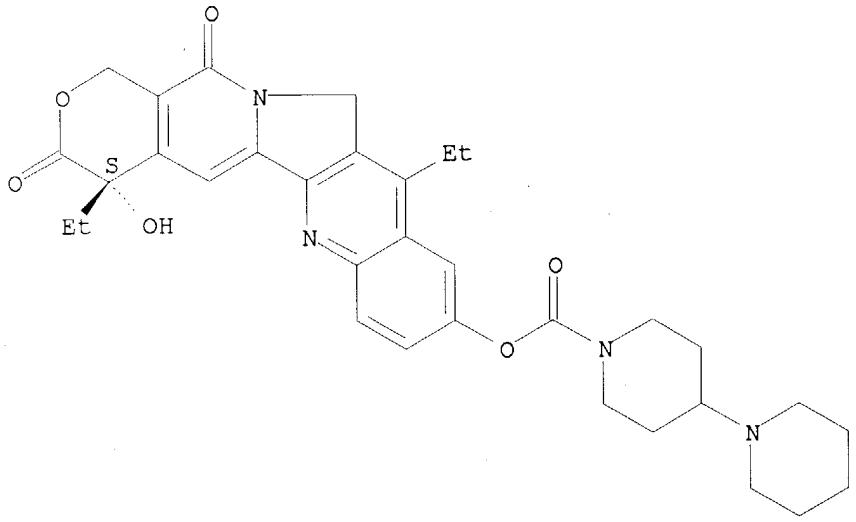
IT 50-07-7, Mitomycin-C 50-18-0, Cyclophosphamide 50-76-0, Dactinomycin 50-91-9 51-21-8, 5-Fluorouracil 51-75-2, Mechlorethamine 55-98-1, Busulfan 57-22-7, Vincristine 59-05-2, Methotrexate 147-94-4, Cytarabine 148-82-3, Melphalan 154-42-7, Thioguanine 154-93-8, Carmustine 305-03-3, Chlorambucil 315-30-0, Allopurinol 427-51-0, Cyproterone acetate 595-33-5, Megestrol acetate 645-05-6, Hexamethylmelamine 865-21-4, Vinblastine 4291-63-8, Cladribine 4342-03-4, Dacarbazine 10540-29-1, Tamoxifen 13010-47-4, Lomustine 13311-84-7, Flutamide 15663-27-1, Cisplatin 18378-89-7, Mithramycin 20830-81-3, Daunomycin 21679-14-1, Fludarabine 23214-92-8, Doxorubicin 31441-78-8, Mercaptopurine 33069-62-4, Paclitaxel 41575-94-4, Carboplatin 53643-48-4, Vindesine 56420-45-2, Epirubicin 58957-92-9, Idarubicin 61825-94-3, Oxaliplatin 63612-50-0, Nilutamide 71486-22-1, Vinorelbine 82413-20-5, Droloxifene 84449-90-1, Raloxifene 89778-26-7, Toremifene 90357-06-5, Bicalutamide 91421-43-1, 9-Amino camptothecin **97682-44-5**, Irinotecan 98319-26-7, Finasteride **100286-90-6**, CPT-11 107868-30-4, Exemestane 112809-51-5, Letrozole 114977-28-5, Docetaxel 120511-73-1, Anastrozole 129731-10-8, Vorozole 145781-92-6, Goserelin acetate 149882-10-0 154039-60-8, Marimastat **169590-42-5**, Celecoxib 531553-45-4, Iodoxyfene
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combined with alkynyl thienopyrimidine protein tyrosine kinase inhibitors useful against cancer and other disorders)

IT **97682-44-5**, Irinotecan **100286-90-6**, CPT-11
169590-42-5, Celecoxib
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combined with alkynyl thienopyrimidine protein tyrosine kinase inhibitors useful against cancer and other disorders)

RN 97682-44-5 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-

b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

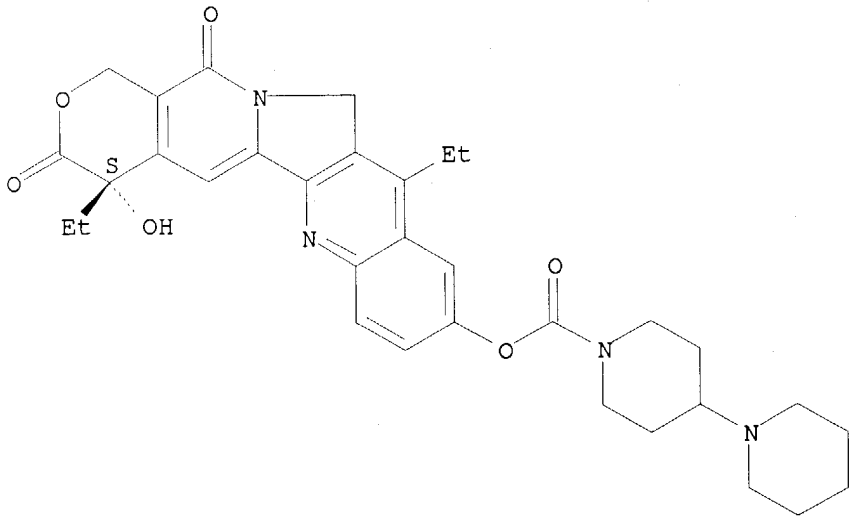
Absolute stereochemistry. Rotation (+).



RN 100286-90-6 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A

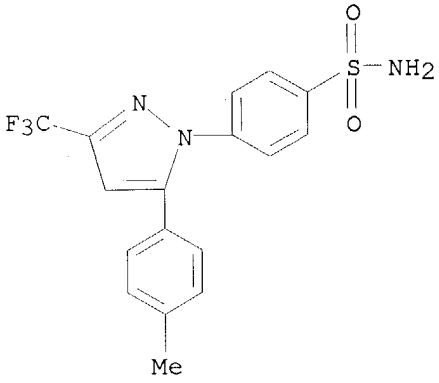


PAGE 2-A

● HCl

● HCl

RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:818745 HCAPLUS
DOCUMENT NUMBER: 138:362256
TITLE: Cyclooxygenase-2 inhibition with celecoxib enhances antitumor efficacy and reduces diarrhea side effect of CPT-11
AUTHOR(S): Trifan, Ovidiu C.; Durham, William F.; Salazar, Valerie S.; Horton, Jennifer; Levine, Benjamin D.; Zweifel, Ben S.; Davis, Thomas W.; Masferrer, Jaime L.
CORPORATE SOURCE: Oncology Pharmacology, Pharmacia Corp., Chesterfield, MO, 63198, USA
SOURCE: Cancer Research (2002), 62(20), 5778-5784
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Combining anticancer drugs with different mechanisms of action has the potential to enhance antitumor effect. CPT-11 (Camptosar, irinotecan), a topoisomerase I inhibitor, has been shown to be highly effective in the treatment of a variety of cancers. However, its clin. usage is often complicated by late diarrhea. A no. of studies have shown that cyclooxygenase (COX)-2 is overexpressed in many forms of human tumors, suggesting that COX-2 inhibition may be useful in the treatment of cancer. In this study, we used two mouse tumor models (HT-29 and colon-26 cells) to evaluate the effect of combining CPT-11 with celecoxib on tumor growth. We also assessed the involvement of COX-2 in the pathogenesis of CPT-11-induced late diarrhea using a rat model. Results indicate that celecoxib enhances the antitumor effect of CPT-11 and reduces the severity of late diarrhea in a dose-dependent manner. The extended benefits of

combining celecoxib with CPT-11 may significantly improve the outcome of cancer patients.

CC 1-6 (Pharmacology)

IT **Antitumor agents**
Diarrhea
Neoplasm
(combination of CPT-11 and celecoxib for cancer therapy and reduced diarrhea)

IT **100286-90-6**, CPT-11
RL: ADV (Adverse effect, including toxicity); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combination of CPT-11 and celecoxib for cancer therapy and reduced diarrhea)

IT **169590-42-5**, Celecoxib
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combination of CPT-11 and celecoxib for cancer therapy and reduced diarrhea)

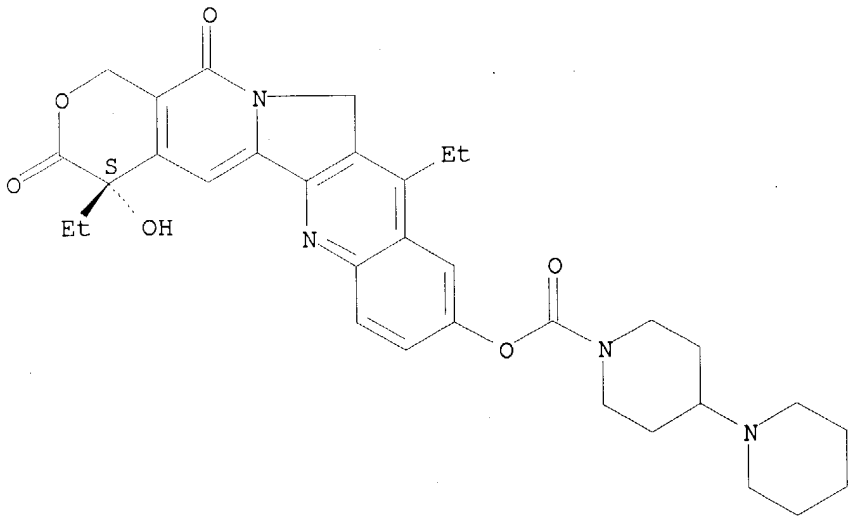
IT **100286-90-6**, CPT-11
RL: ADV (Adverse effect, including toxicity); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combination of CPT-11 and celecoxib for cancer therapy and reduced diarrhea)

RN 100286-90-6 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

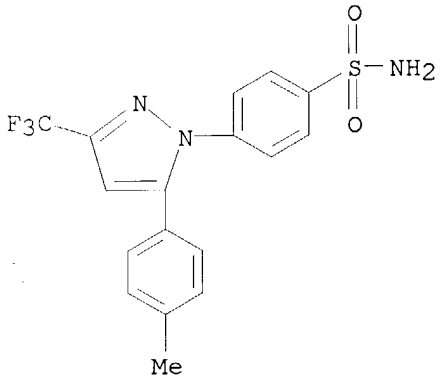
Absolute stereochemistry. Rotation (+).

PAGE 1-A



● HCl

IT **169590-42-5**, Celecoxib
RL: **PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combination of CPT-11 and celecoxib for cancer therapy and reduced diarrhea)
RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:575747 HCAPLUS
DOCUMENT NUMBER: 137:135070
TITLE: DNA topoisomerase I inhibitor-cyclooxygenase 2 inhibitor antiangiogenic combination for the treatment of cancer
INVENTOR(S): McKearn, John P.; Gordon, Gary B.; Cunningham, James; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 97 pp., Cont.-in-part of U.S. Ser. No. 470,951.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 17
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002103141	A1	20020801	US 2001-843132	20010425
WO 2002085459	A2	20021031	WO 2002-US13219	20020425

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
US 1999-470951 A2 19991222
US 2001-843132 A 20010425

OTHER SOURCE(S): MARPAT 137:135070

AB The invention provides combinations of a DNA topoisomerase I inhibiting agent and a selective COX-2 inhibiting agent for preventing, treating, and/or reducing the risk of developing a neoplasia disorder in a mammal. Compd. prepn. is included.

IC ICM A61K031-706
ICS A61K031-4745; A61K031-473; A61K031-407; A61K031-415; A61K031-277

NCL 514043000

CC 1-6 (Pharmacology)
Section cross-reference(s): 27

IT Antidiarrheals
Antitumor agents
Diarrhea
Drug delivery systems
Human
Resolution (separation)
(DNA topoisomerase I inhibitor-cyclooxygenase 2 inhibitor antiangiogenic combination for treatment of cancer)

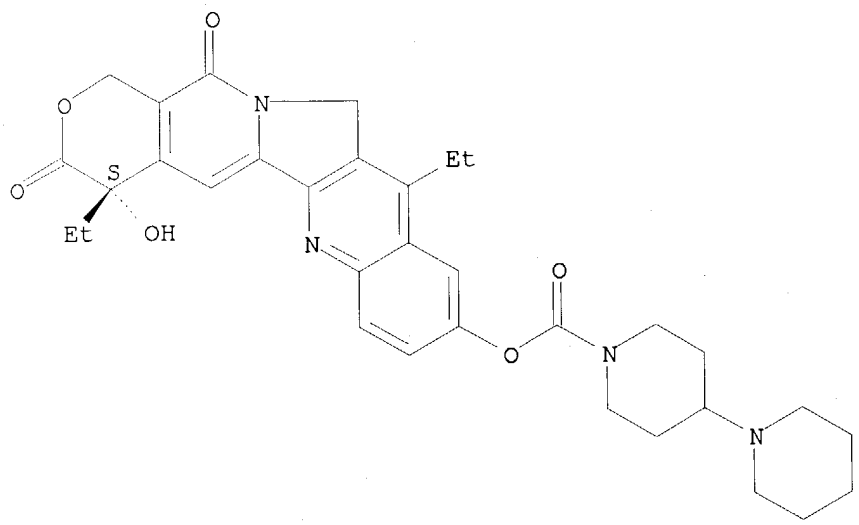
IT 254-04-6D, 2H-1-Benzopyran, derivs. 7689-03-4, Camptothecin 51803-78-2 71125-38-7, Meloxicam 80937-31-1 89458-99-1 89459-25-6 91421-42-0, 9-Nitrocamptothecin 91421-43-1, 9-Aminocamptothecin 93014-16-5 **97682-44-5**, Irinotecan **100286-90-6**, Irinotecan hydrochloride 118458-54-1 119413-54-6, Topotecan hydrochloride 123653-11-2 123663-49-0 123948-87-8, Topotecan 133550-30-8 149882-10-0, Lurtotecan 155773-58-3, Lurtotecan dihydrochloride 158205-05-1 158959-32-1 162011-90-7, Rofecoxib 162054-19-5 169590-41-4, Deracoxib **169590-42-5**, Celecoxib 169869-90-3, Exatecan mesylate 170569-86-5 170569-88-7 170570-29-3 170630-33-8 172889-50-8 177660-77-4 177660-95-6 178816-61-0 178816-94-9, [1,1':2',1''-Terphenyl]-4-sulfonamide 179382-91-3 180200-68-4 181485-41-6 181695-72-7, Valdecoxib 181695-81-8 181696-33-3 187845-71-2 187845-80-3 187846-16-8 189954-13-0 189954-16-3 197239-97-7 197239-99-9 197240-09-8 197240-14-5 198470-84-7 202409-33-4, Etoricoxib 203923-89-1, Karenitecin 212126-32-4 215122-12-6 215122-19-3 215122-20-6 215122-24-0 215122-27-3 215122-28-4 215122-29-5 215122-30-8 215122-31-9 215122-32-0 215122-33-1 215122-35-3 215122-36-4 215122-39-7 215122-44-4 215122-45-5 215122-46-6 215122-48-8 215122-49-9 215122-50-2 215122-51-3 215122-52-4 215122-53-5 215122-55-7 215122-56-8 215122-58-0 215122-59-1 215122-60-4 215122-61-5 215122-62-6 215122-63-7 215122-65-9 215122-68-2 215122-70-6 215122-71-7 215122-75-1 215122-76-2 215122-77-3 215123-07-2 215123-08-3 215123-16-3 215123-84-5 226703-01-1 266320-83-6 279221-13-5 279221-14-6 279221-15-7 279221-17-9 303090-18-8 444576-88-9
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(DNA topoisomerase I inhibitor-cyclooxygenase 2 inhibitor antiangiogenic combination for treatment of cancer)

IT **97682-44-5**, Irinotecan **100286-90-6**, Irinotecan hydrochloride **169590-42-5**, Celecoxib
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(DNA topoisomerase I inhibitor-cyclooxygenase 2 inhibitor antiangiogenic combination for treatment of cancer)

RN 97682-44-5 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

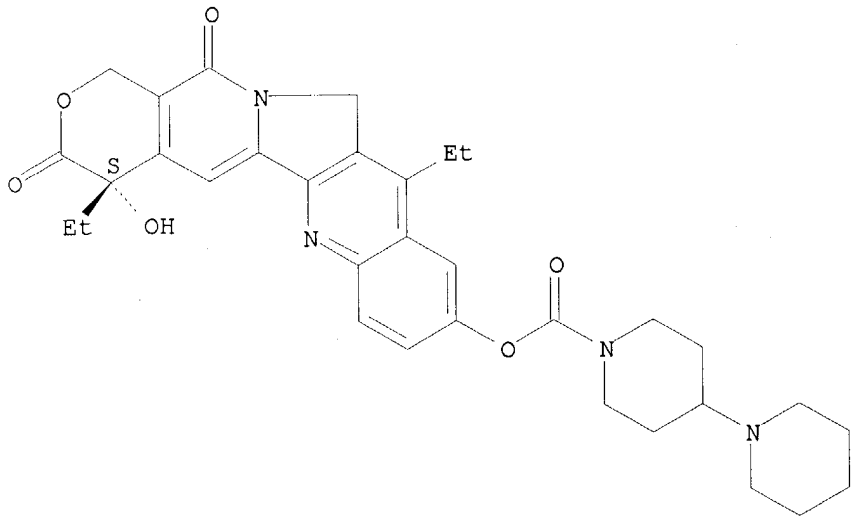
Absolute stereochemistry. Rotation (+).



RN 100286-90-6 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

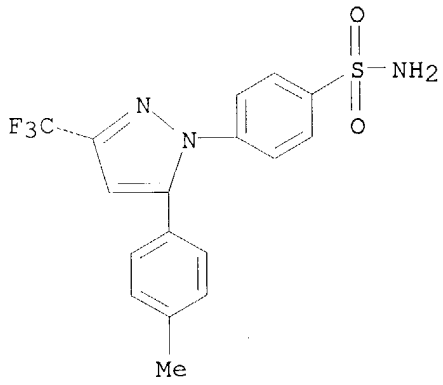
PAGE 1-A



PAGE 2-A

● HCl

RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L13 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:396644 HCAPLUS
DOCUMENT NUMBER: 135:24671
TITLE: Solid carriers for improved delivery of active ingredients in pharmaceutical compositions
INVENTOR(S): Patel, Manesh V.; Chen, Feng-jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 107 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037808	A1	20010531	WO 2000-US32255	20001122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6248363	B1	20010619	US 1999-447690	19991123
EP 1233756	A1	20020828	EP 2000-980761	20001122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003517470	T2	20030527	JP 2001-539423	20001122

PRIORITY APPLN. INFO.: US 1999-447690 A 19991123
WO 2000-US32255 W 20001122

AB The present invention provides solid pharmaceutical compns. for improved delivery of a wide variety of pharmaceutical active ingredients contained therein or sep. administered. In one embodiment, the solid pharmaceutical compn. includes a solid carrier, the solid carrier including a substrate and an encapsulation coat on the substrate. The encapsulation coat can include different combinations of pharmaceutical active ingredients, hydrophilic surfactant, lipophilic surfactants and triglycerides. In another embodiment, the solid pharmaceutical compn. includes a solid carrier, the solid carrier being formed of different combinations of pharmaceutical active ingredients, hydrophilic surfactants, lipophilic surfactants and triglycerides. The compns. of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritionals, cosmeceuticals and diagnostic agents. A compn. contained glyburide 1, PEG 40 stearate 33, glycerol monolaurate 17, and nonpareil seed 80 g.

IC ICM A61K009-14
ICS A61K009-16; A61K009-20; A61K009-46; A61K009-48; A61K009-50; A61K009-54

CC 63-6 (Pharmaceuticals)

IT Analgesics
Anti-inflammatory agents
Anticoagulants
Anticonvulsants
Antidepressants
Antidiabetic agents
Antihistamines
Antihypertensives
Antimalarials
Antipsychotics
Antitumor agents
Anxiolytics
Fungicides

Hypnotics and Sedatives
Immunosuppressants
Muscarinic antagonists
Muscle relaxants
Plasticizers
Protozoacides
Sweetening agents
Tranquilizers
Vaccines
(solid carriers for improved delivery of active ingredients in pharmaceutical compns.)

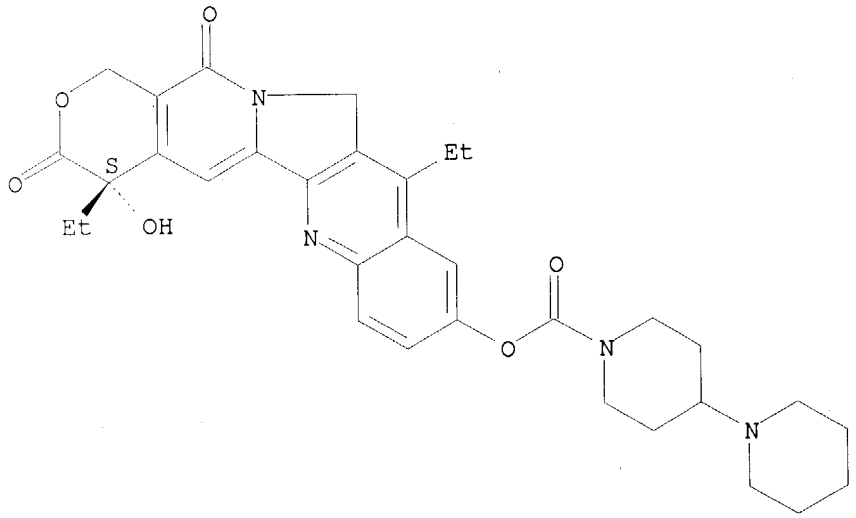
IT 69049-74-7, Nedocromil sodium 69655-05-6, Didanosine 69756-53-2, Halofantrine 70288-86-7, Ivermectin 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 71486-22-1, Vinorelbine 72432-03-2, Miglitol 72559-06-9, Rifabutine 73384-59-5, Ceftriaxone 73590-58-6, Omeprazole 73963-72-1, Cilostazol 74011-58-8, Enoxacin 74103-06-3, Ketorolac 74356-00-6, Cefotetan disodium 74381-53-6, Leuprolide acetate 75330-75-5, Lovastatin 75706-12-6, Leflunomide 76420-72-9, Enalaprilat 76470-66-1, Loracarbef 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine 78110-38-0, Aztreonam 79350-37-1, Cefixime 79517-01-4, Octreotide acetate 79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin 81093-37-0, Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin 81161-17-3, Esmolol hydrochloride 82410-32-0, Ganciclovir 82419-36-1, Ofloxacin 82626-48-0, Zolpidem 82952-64-5, Trimetrexate glucuronate 83799-24-0, Fexofenadine 83869-56-1, Granulocyte-macrophage colony stimulating factor 83881-51-0, Cetirizine 83905-01-5, Azithromycin 84057-84-1, Lamotrigine 84371-65-3, Mifepristone 84449-90-1, Raloxifene 84625-61-6, Itraconazole 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5, Benazepril 87679-37-6, Trandolapril 88150-42-9, Amlodipine 88669-04-9, Trospectomycin 89778-26-7, Toremifene 89987-06-4, Tiludronate 90357-06-5, Bicalutamide 91161-71-6, Terbinafine 93390-81-9, Fosphenytoin 93413-69-5, Venlafaxine 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 94749-08-3, Salmeterol xinafoate 95233-18-4, Atovaquone 97240-79-4, Topiramate 97322-87-7, Troglitazone **97682-44-5**, Irinotecan 98079-51-7, Lomefloxacin 98319-26-7, Finasteride 100986-85-4, Levofloxacin 101828-21-1, Butenafine 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 104227-87-4, Famciclovir 104987-11-3, Tacrolimus 105462-24-6, Risedronic acid 106133-20-4, Tamsulosin 106392-12-5, Oxirane, polymer with methyloxirane, block 106650-56-0, Sibutramine 106819-53-8, Doxacurium chloride 106861-44-3, Mivacurium chloride 107648-80-6, Cefepime hydrochloride 107753-78-6, Zafirlukast 109319-16-6, Factor VIII 110871-86-8, Sparfloxacin 111025-46-8, Pioglitazone 111406-87-2, Zileuton 112965-21-6, Calcipotriene 113427-24-0 113665-84-2, Clopidogrel 113852-37-2, Cidofovir 115103-54-3, Tiagabine 116094-23-6, Insulin aspart 117976-89-3, Rabeprazole 118072-93-8, Zoledronate 118292-40-3, Tazarotene 119914-60-2, Grepafloxacin 120014-06-4, Donepezil 121368-58-9, Olpadronate 121679-13-8, Naratriptan 122320-73-4, Rosiglitazone 123948-87-8, Topotecan 124832-26-4, Valaciclovir 127759-89-1, Lobucavir 127779-20-8, Saquinavir 129497-78-5, Verteporfin 131918-61-1, Paricalcitol 133040-01-4, Eprosartan 133107-64-9, Insulin lispro 134523-00-5, Atorvastatin 134678-17-4, Lamivudine 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 139110-80-8, Zanamivir 139264-17-8, Zolmitriptan 139481-59-7, Candesartan 139639-23-9, Tissue type plasminogen activator

142128-59-4, Terzolin 143003-46-7, Alglucerase 143011-72-7, Granulocyte colony stimulating factor 143831-71-4 144034-80-0, Rizatriptan 144494-65-5, Tirofiban 144701-48-4, Telmisartan 145599-86-6, Cerivastatin 145941-26-0, Oprelvekin 146961-76-4, Alatrofloxacin 147059-72-1, Trovafloxacin 148553-50-8, Pregabalin 151126-32-8, Pramlintide 153559-49-0, Targretin 154361-50-9, Capecitabine 154598-52-4, Efavirenz 155213-67-5, Ritonavir 157810-81-6, Indinavir sulfate 158747-02-5, Frovatriptan 158966-92-8, Montelukast 159989-64-7, Nelfinavir 160337-95-1, Insulin glargine 162011-90-7, Rofecoxib 165101-51-9, Becaplermin 169148-63-4, Insulin detemir **169590-42-5**, Celecoxib 171599-83-0, Sildenafil citrate 173146-27-5, Denileukin diftitox 191588-94-0, TNK-tPA
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(solid carriers for improved delivery of active ingredients in pharmaceutical compns.)

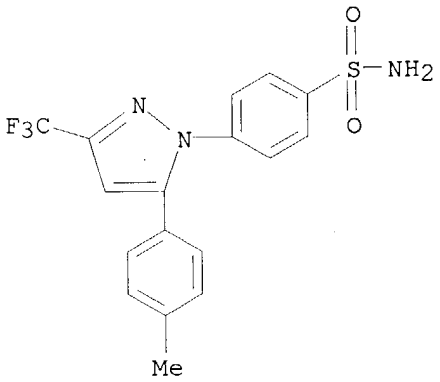
IT **97682-44-5**, Irinotecan **169590-42-5**, Celecoxib
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(solid carriers for improved delivery of active ingredients in pharmaceutical compns.)

RN 97682-44-5 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:319727 HCAPLUS
DOCUMENT NUMBER: 134:316158
TITLE: Oral formulations for camptothecin antitumor compounds
INVENTOR(S): Muggetti, Lorena; Martini, Alessandro; Civaroli, Paola; James, Christopher
PATENT ASSIGNEE(S): Pharmacia & Upjohn S.p.A., Italy
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030351	A1	20010503	WO 2000-EP9647	20001002
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000014902	A	20020611	BR 2000-14902	20001002
EP 1223936	A1	20020724	EP 2000-966102	20001002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003512430	T2	20030402	JP 2001-532771	20001002
NO 2002001834	A	20020418	NO 2002-1834	20020418

PRIORITY APPLN. INFO.: GB 1999-25127 A 19991022
WO 2000-EP9647 W 20001002

AB The present invention relates to a semi-solid filling medium which comprises a camptothecin deriv.; a pharmaceutically acceptable carrier matrix which is a polyglycolized glyceride; and an effective thickening-reducing and stabilizing-promoting amt. of one or more pharmaceutically acceptable excipients. For example, a capsule

formulation contg. 50 mg of CPT-11 dispersed in a mixt. of Gelucire 44/14 and Epikuron 135F was prepd. showing good dissoln. and stability.

IC ICM A61K031-47
ICS A61K009-48

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2

IT **Antitumor agents**
(antibiotic; oral formulations for camptothecin antitumor compds.)

IT Alkylating agents, biological
Angiogenesis inhibitors
Antitumor agents
Chelating agents
Dispersing agents
Solubilizers
Surfactants
(oral formulations for camptothecin antitumor compds.)

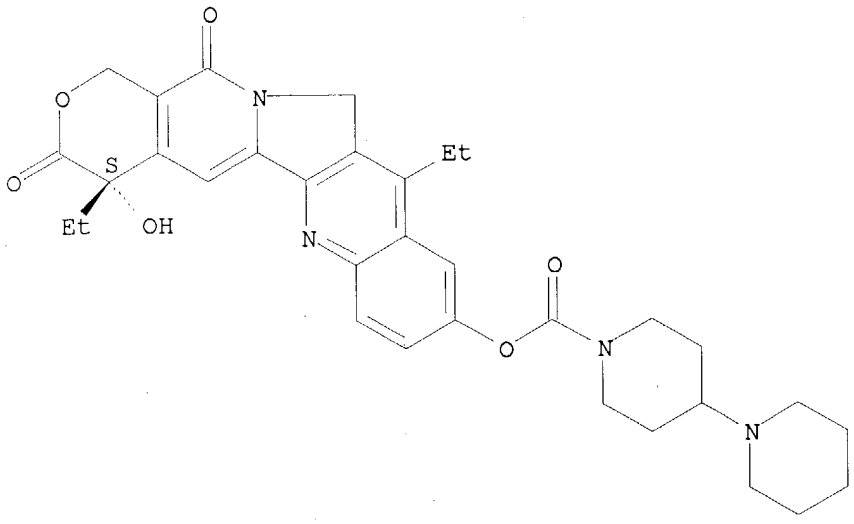
IT 50-35-1, Thalidomide 56-85-9, Glutamine, biological studies 58-05-9, Leucovorin 4891-15-0, Estramustine phosphate 7440-06-4D, Platinum, compds., biological studies 10540-29-1, Tamoxifen 15663-27-1, Cisplatin 33069-62-4, Paclitaxel 41575-94-4, Carboplatin 61825-94-3, Oxaliplatin 78287-27-1, SN-22 83150-76-9, Octreotide 86639-52-3, SN 38 91421-42-0, 9-Nitro-20(S)-camptothecin 91421-43-1, 9-Amino-20(S)-camptothecin **100286-90-6**, CPT-11 114977-28-5, Docetaxel 119413-54-6, Topotecan hydrochloride 154361-50-9, Capecitabine 162011-90-7, Rofecoxib **169590-42-5**, Celecoxib 181695-72-7, Valdecoxib 198470-84-7, Parecoxib 204005-46-9, SU 5416 252916-29-3, SU 6668
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(oral formulations for camptothecin antitumor compds.)

IT **100286-90-6**, CPT-11 **169590-42-5**, Celecoxib
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(oral formulations for camptothecin antitumor compds.)

RN 100286-90-6 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

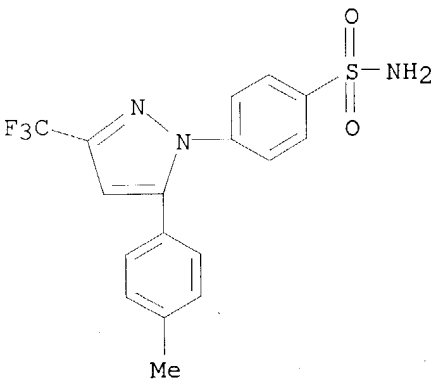
PAGE 1-A



PAGE 2-A

● HCl

RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:608551 HCAPLUS
DOCUMENT NUMBER: 133:213151
TITLE: Pharmaceutical compositions and methods for improved delivery of hydrophobic therapeutic agents
INVENTOR(S): Patel, Manesh V.; Chen, Feng-Jing

PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050007	A1	20000831	WO 2000-US165	20000105
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6294192	B1	20010925	US 1999-258654	19990226
NZ 513810	A	20010928	NZ 2000-513810	20000105
EP 1158959	A1	20011205	EP 2000-901394	20000105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537317	T2	20021105	JP 2000-600619	20000105

PRIORITY APPLN. INFO.: US 1999-258654 A 19990226
WO 2000-US165 W 20000105

AB The present invention relates to triglyceride-free pharmaceutical compns. for delivery of hydrophobic therapeutic agents. Compns. of the present invention include a hydrophobic therapeutic agent and a carrier, where the carrier is formed from a combination of a hydrophilic surfactant and a hydrophobic surfactant. Upon diln. with an aq. solvent, the compn. forms a clear, aq. dispersion of the surfactants contg. the therapeutic agent. The invention also provides methods of treatment with hydrophobic therapeutic agents using these compns. A pharmaceutical compn. contained cyclosporin 0.14, Cremophor RH-40 0.41, Arlacel186 0.29, sodium taurocholate 0.26, and propylene glycol 0.46 mg.

IC ICM A61K009-127
ICS A61K009-107; A61K038-13

CC 63-6 (Pharmaceuticals)

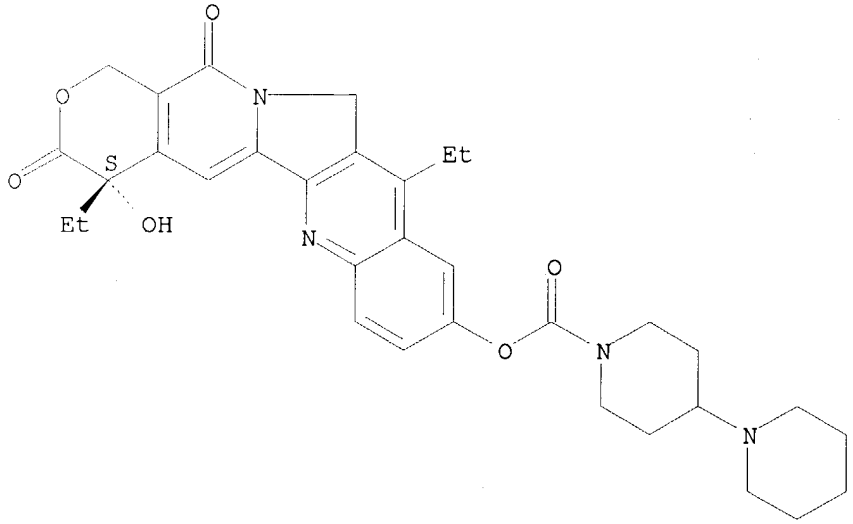
IT Analgesics
Anthelmintics
Anti-inflammatory agents
Antianginal agents
Antiarrhythmics
Antibacterial agents
Anticoagulants
Anticonvulsants
Antidepressants
Antidiabetic agents
Antihistamines
Antihypertensives
Antimalarials
Antimigraine agents
Antiobesity agents
Antiparkinsonian agents

Antipsychotics
Antitumor agents
Antiviral agents
Anxiolytics
Cognition enhancers
Diuretics
Fungicides
Hypnotics and Sedatives
Immunosuppressants
Inotropics
Muscarinic antagonists
Muscle relaxants
Nervous system stimulants
Nutrition, animal
Protozoacides
Thyroid gland
(pharmaceutical compns. and methods for improved delivery of hydrophobic therapeutic agents)

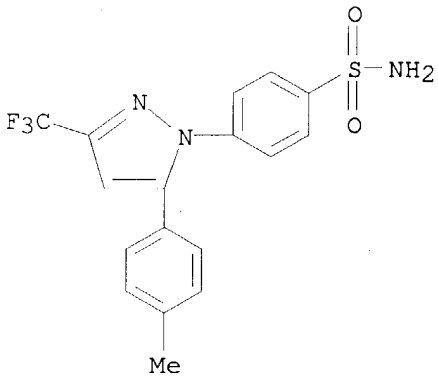
IT 68958-64-5, Polyoxyethylene glyceryl trioleate 69756-53-2, Halofantrine 70288-86-7, Ivermectin 72432-03-2, Miglitol 72559-06-9, Rifabutine 73590-58-6, Omeprazole 73963-72-1, Cilostazol 74103-06-3, Ketorolac 74504-64-6, Polyglyceryl laurate 75706-12-6, Leflunomide 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine 79217-60-0, Cyclosporin 79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin 81093-37-0, Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin 82626-48-0, Zolpidem 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83905-01-5, Azithromycin 84057-84-1, Lamotrigine 84371-65-3, Mifepristone 84449-90-1, Raloxifene 84625-61-6, Itraconazole 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5, Benazepril 86637-84-5 88150-42-9, Amlodipine 89778-26-7, Toremifene 90357-06-5, Bicalutamide 91161-71-6, Terbinafine 93390-81-9, Fosphenytoin 93413-69-5, Venlafaxine 93479-97-1, Glimepiride 93790-70-6, Cholylsarcosine 93790-72-8 93957-54-1, Fluvastatin 95233-18-4, Atovaquone 97240-79-4, Topiramate 97322-87-7, Troglitazone **97682-44-5**, Irinotecan 98319-26-7, Finasteride 101828-21-1, Butenafine 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 104987-11-3, Tacrolimus 106133-20-4, Tamsulosin 106392-12-5, Ethylene oxide propylene oxide block copolymer 106650-56-0, Sibutramine 107753-78-6, Zafirlukast 111025-46-8, Pioglitazone 111406-87-2, Zileuton 112965-21-6, Calcipotriene 113665-84-2, Clopidogrel 115103-54-3, Tiagabine 117976-89-3, Rabeprazole 118292-40-3, Tazarotene 120014-06-4, Donepezil 121679-13-8, Naratriptan 122320-73-4, Rosiglitazone 123948-87-8, Topotecan 127779-20-8, Saquinavir 129497-78-5, Verteporfin 131918-61-1, Paricalcitol 133040-01-4, Eprosartan 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6 139264-17-8, Zolmitriptan 139481-59-7, Candesartan 144034-80-0, Rizatriptan 144494-65-5, Tirofiban 144701-48-4, Telmisartan 145599-86-6, Cerivastatin 145941-26-0, Oprelvekin 147059-72-1, Trovafloxacin 150372-93-3, Polyoxyethylene glyceryl laurate 153559-49-0, Targretin 154598-52-4, Efavirenz 155213-67-5, Ritonavir 156259-68-6, Capmul mcm 158747-02-5, Frovatriptan 158966-92-8, Montelukast 159989-64-7, Nelfinavir 162011-90-7, Rofecoxib **169590-42-5**, Celecoxib 171599-83-0, Sildenafil citrate
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical compns. and methods for improved delivery of

hydrophobic therapeutic agents)
IT **97682-44-5**, Irinotecan **169590-42-5**, Celecoxib
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical compns. and methods for improved delivery of hydrophobic therapeutic agents)
RN 97682-44-5 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:456950 HCAPLUS

DOCUMENT NUMBER: 133:84244
TITLE: Method of using a cyclooxygenase-2 inhibitor and an integrin antagonist as a combination therapy in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA
SOURCE: PCT Int. Appl., 348 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 17
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038786	A2	20000706	WO 1999-US30692	19991222
WO 2000038786	A3	20010308		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356302	AA	20000706	CA 1999-2356302	19991222
EP 1140179	A2	20011010	EP 1999-966594	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533422	T2	20021008	JP 2000-590734	19991222
ZA 2001005055	A	20020920	ZA 2001-5055	20010620
ZA 2001005120	A	20020107	ZA 2001-5120	20010621

PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30692 W 19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a cyclooxygenase-2 inhibitor, an integrin antagonist and an antineoplastic agent.
IC ICM A61P041-00
ICS A61P035-00; A61K045-06
CC 1-6 (Pharmacology)
IT **Antitumor agents**
(Ewing's sarcoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)
IT **Antitumor agents**
(Leydig cell tumor; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)
IT **Antitumor agents**
(Wilms' tumor; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)
IT **Antitumor agents**
(adenocarcinoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)
IT **Antitumor agents**
(astrocytoma; cyclooxygenase-2 inhibitor and integrin antagonist in

combination for neoplasia treatment)

IT **Antitumor agents**
(basal cell carcinoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(bladder carcinoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(bronchi carcinoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(carcinoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(carcinosarcoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(cervix; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(cholangioma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(chondrosarcoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(choroid plexus papilloma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(colon carcinoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(colon; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT Angiogenesis inhibitors
Antitumor agents
Carcinoid
Drug interactions
Radiotherapy
(cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(digestive tract; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(germinoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(glioblastoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(glucagonoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(head; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**

(hemangioma, inhibitors; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(hepatoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(insulinoma, inhibitors; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(leiomyosarcoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(lentigo maligna melanoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(lung small-cell carcinoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(lung, metastasis; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
Antitumor agents
(lung, pulmonary blastoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
Antitumor agents
(lung; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(mammary gland carcinoma, metastasis; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(mammary gland; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(medulloblastoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(melanoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(meninges; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(mesothelioma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(metastasis; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(mucoepidermoid carcinoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(multiple myeloma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(neck; cyclooxygenase-2 inhibitor and integrin antagonist in

combination for neoplasia treatment)

IT **Antitumor agents**
(neuroblastoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(oligodendroglioma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(osteosarcoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(ovary carcinoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
Antitumor agents
(pancreas; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(pinealoma inhibitors; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(renal cell carcinoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(retinoblastoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(rhabdomyosarcoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(sarcoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(soft tissue, carcinoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(squamous cell carcinoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **Antitumor agents**
(uvea melanoma; cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT 51-21-8, 5-Fluorouracil 52-24-4, Thiotepa 57-22-7, Vincristine 58-05-9, Leucovorin 76-43-7, Fluoxymesterone 128-13-2, Ursodeoxycholic acid 154-93-8, BCNU 302-79-4, Retinoic acid 471-34-1, Calcium carbonate, biological studies 865-21-4, Vinblastine 1464-42-2, Selenomethionine 3562-63-8, Megestrol 7782-49-2, Selenium, biological studies 10540-29-1, Tamoxifen 14769-73-4, Levamisole 15663-27-1, Cisplatin 23214-92-8, Doxorubicin 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin 51803-78-2 59973-80-7, Sulindac sulfone 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 65807-02-5, Goserelin 70052-12-9, Eflornithine 71486-22-1, Vinorelbine 80937-31-1 84449-90-1, Raloxifene 89778-26-7, Toremifene 93014-16-5 95058-81-4, Gemcitabine **97682-44-5**, Irinotecan 107868-30-4, Exemestane 112809-51-5, Letrozole 114977-28-5, Docetaxel 120511-73-1, Anastrozole 123653-11-2 123663-49-0 123948-87-8, Topotecan 154361-50-9, Capecitabine 158205-05-1 158959-32-1 162011-90-7, Rofecoxib 162054-19-5 **169590-42-5** 170569-86-5

170569-87-6 170569-88-7 170570-29-3 174664-91-6 175529-44-9
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[1,1':2',1''-Terphenyl]-4-sulfonamide 179382-91-3 180200-68-4, JTE-522
181485-41-6 181695-72-7 181695-81-8 181696-33-3 187845-71-2
187845-80-3 187846-16-8 188968-51-6, EMD-121974 189954-13-0
189954-16-3 193532-75-1 197239-97-7 197239-99-9 197240-09-8
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227751-60-2 243640-62-2 251972-30-2, SC-58236 279221-12-4
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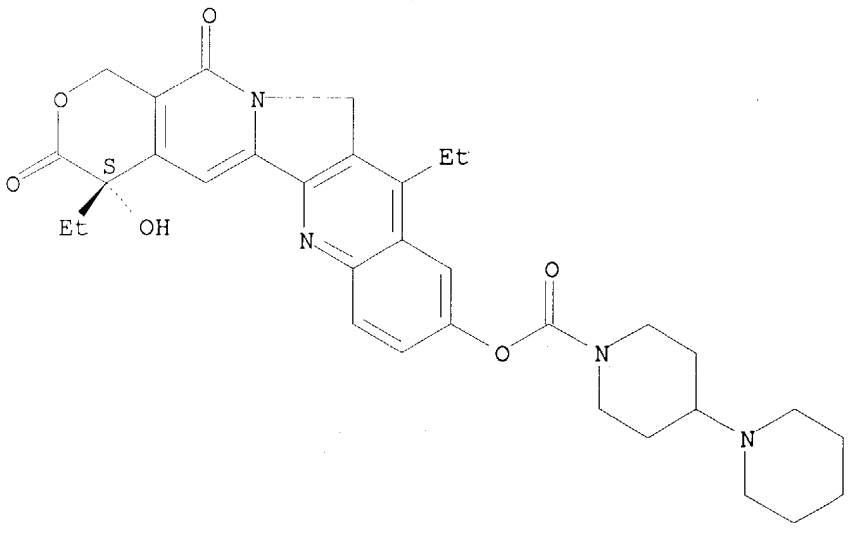
280105-29-5 280105-30-8 280105-31-9 280123-02-6 280123-03-7
280763-79-3 280763-80-6 280763-81-7 280763-82-8 280763-83-9
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

IT **97682-44-5**, Irinotecan **169590-42-5**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor and integrin antagonist in combination for neoplasia treatment)

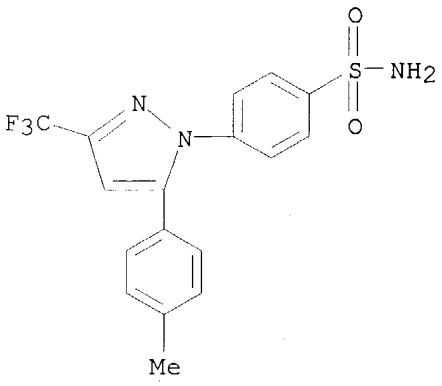
RN 97682-44-5 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-

yl]- (9CI) (CA INDEX NAME)



L13 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:456927 HCAPLUS
DOCUMENT NUMBER: 133:84243
TITLE: Method of using a cyclooxygenase-2 inhibitor and one or more antineoplastic agents as a combination therapy in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 236 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 17
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038730	A2	20000706	WO 1999-US30693	19991222
WO 2000038730	A3	20001102		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356606	AA	20000706	CA 1999-2356606	19991222
EP 1140192	A2	20011010	EP 1999-967543	19991222
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BR 9916518	A	20020129	BR 1999-16518	19991222
JP 2002533416	T2	20021008	JP 2000-590681	19991222
ZA 2001005055	A	20020920	ZA 2001-5055	20010620
ZA 2001005120	A	20020107	ZA 2001-5120	20010621

NO 2001003155	A	20010822	NO 2001-3155		20010622
US 2003119895	A1	20030626	US 2002-150546		20020516
US 2003203956	A1	20031030	US 2002-212523		20020805
PRIORITY APPLN. INFO.:			US 1998-113786P	P	19981223
			WO 1999-US30693	W	19991222
			US 2001-857873	A2	20011005

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a cyclooxygenase-2 inhibitor and an antineoplastic agent.

IC ICM A61K045-06
ICS A61K041-00; A61P035-00

CC 1-6 (Pharmacology)

IT **Antitumor agents**
(Ewing's sarcoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(Wilms' tumor; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(adenocarcinoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(astrocytoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(basal cell carcinoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(bladder carcinoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(bronchi carcinoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(carcinoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(carcinosarcoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(cervix; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(cholangioma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(chondrosarcoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(choroid plexus papilloma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(colon; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
Carcinoid
Drug interactions

Radiotherapy
(cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(digestive tract; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(germinoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(glioblastoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(glucagonoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(head; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(hemangioma, inhibitors; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(hepatoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(insulinoma, inhibitors; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(leiomyosarcoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(lentigo maligna melanoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(lung small-cell carcinoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(lung, metastasis; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
Antitumor agents
(lung, pulmonary blastoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
Antitumor agents
(lung; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(mammary gland; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(medulloblastoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(melanoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**

(meninges; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(mesothelioma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(metastasis; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(mucoepidermoid carcinoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(multiple myeloma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(neck; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(neuroblastoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(oligodendroglioma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(osteosarcoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
Antitumor agents
(pancreas; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(pinealoma inhibitors; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(renal cell carcinoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(retinoblastoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(rhabdomyosarcoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(sarcoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(soft tissue, carcinoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(squamous cell carcinoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT **Antitumor agents**
(uvea melanoma; cyclooxygenase-2 inhibitor-antineoplastic agent combination for neoplasia treatment)

IT 51-21-8, 5-Fluorouracil 52-24-4, Thiotepa 53-86-1, Indomethacin 57-22-7, Vincristine 58-05-9, Leucovorin 76-43-7, Fluoxymesterone 302-79-4, Retinoic acid 471-34-1, Calcium carbonate, biological studies

865-21-4, Vinblastine 1464-42-2, Selenomethionine 3562-63-8, Megestrol
7782-49-2, Selenium, biological studies 10540-29-1, Tamoxifen
14769-73-4, Levamisole 15663-27-1, Cisplatin 23214-92-8, Doxorubicin
33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin
51803-78-2 59973-80-7, Sulindac sulfone 65271-80-9, Mitoxantrone
65277-42-1, Ketoconazole 65807-02-5, Goserelin 70052-12-9,
Eflornithine 71486-22-1, Vinorelbine 80937-31-1 84449-90-1,
Raloxifene 89778-26-7, Toremifene 93014-16-5 95058-81-4, Gemcitabine
97682-44-5, Irinotecan 107868-30-4, Exemestane 112809-51-5,
Letrozole 114977-28-5, Docetaxel 120511-73-1, Anastrozole
123653-11-2 123663-49-0 123948-87-8, Topotecan 154361-50-9,
Capecitabine 158205-05-1 158959-32-1 162011-90-7, Rofecoxib
162054-19-5 **169590-42-5**, Celecoxib 170569-86-5 170569-87-6
170569-88-7 170570-29-3 177660-77-4 177660-95-6 178816-61-0
178816-94-9, [1,1':2',1''-Terphenyl]-4-sulfonamide 179382-91-3
180200-68-4, JTE 522 181485-41-6 181695-72-7, Valdecoxib 181695-81-8
181696-33-3 187845-71-2 187845-80-3 187846-16-8 189954-13-0
189954-16-3 197239-97-7 197239-99-9 197240-09-8 197240-14-5
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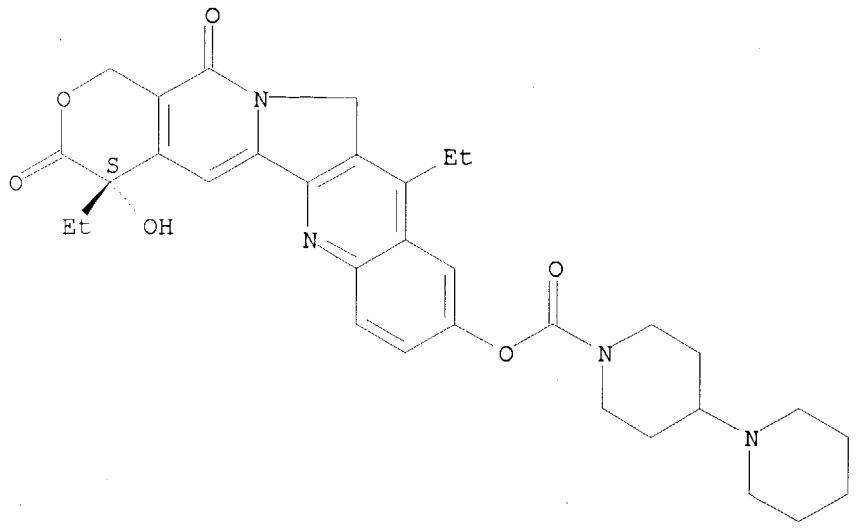
226703-01-1 227619-96-7, CP 461 251972-30-2, SC-58236 279221-12-4
279221-13-5 279221-14-6 279221-15-7 279221-17-9 279221-18-0
279221-19-1
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor-antineoplastic agent combination for
neoplasia treatment)

IT **97682-44-5**, Irinotecan **169590-42-5**, Celecoxib
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor-antineoplastic agent combination for
neoplasia treatment)

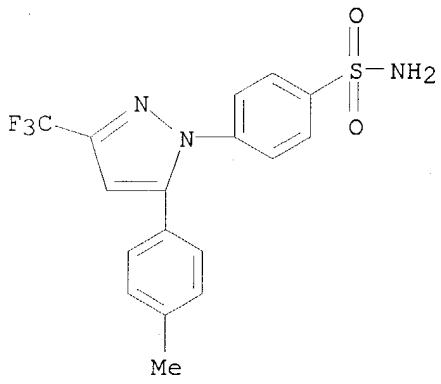
RN 97682-44-5 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L13 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:441655 HCAPLUS
DOCUMENT NUMBER: 133:68922
TITLE: Method of using a cyclooxygenase-2 inhibitor and a matrix metalloproteinase inhibitor as a combination therapy in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA
SOURCE: PCT Int. Appl., 437 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 17
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037107	A2	20000629	WO 1999-US30776	19991222
WO 2000037107	A3	20010201		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356426	AA	20000629	CA 1999-2356426	19991222
EP 1140194	A2	20011010	EP 1999-968540	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9916536	A	20020102	BR 1999-16536	19991222
JP 2002532563	T2	20021002	JP 2000-589217	19991222
ZA 2001005055	A	20020920	ZA 2001-5055	20010620
ZA 2001005120	A	20020107	ZA 2001-5120	20010621
NO 2001003156	A	20010823	NO 2001-3156	20010622
PRIORITY APPLN. INFO.:			US 1998-113786P P	19981223
			WO 1999-US30776 W	19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a cyclooxygenase-2 inhibitor, a matrix metalloproteinase inhibitor and an antineoplastic agent.

IC ICM A61K045-06
ICS A61P035-00; A61K041-00

CC 1-6 (Pharmacology)

IT **Antitumor agents**
(Ewing's sarcoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(Wilms' tumor; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(adenocarcinoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(astrocytoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(basal cell carcinoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(bladder carcinoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(bronchi carcinoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(carcinoma, adenoid cystic carcinoma and others; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(carcinosarcoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(cervix; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(cholangioma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(chondrosarcoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(choroid plexus papilloma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(colon carcinoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
Carcinoid
Drug interactions
Hyperplasia
Radiotherapy
(cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(digestive tract; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(glioblastoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(glucagonoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(head; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(hemangioma, inhibitors; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(hepatoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(insulinoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**

(leiomyosarcoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(lentigo maligna melanoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(lung small-cell carcinoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(lung, metastasis; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
Antitumor agents
(lung; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(mammary gland; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(medulloblastoma, and medulloepithelioma inhibitors; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(melanoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(meninges; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(mesothelioma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(metastasis; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(mucoepidermoid carcinoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(multiple myeloma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(neck; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(neuroblastoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(oligodendroglioma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**

(osteosarcoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
Antitumor agents
(pancreas; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(pinealoma inhibitors; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(renal cell carcinoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(retinoblastoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(rhabdomyosarcoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(sarcoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(squamous cell carcinoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

IT **Antitumor agents**
(uvea melanoma; cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

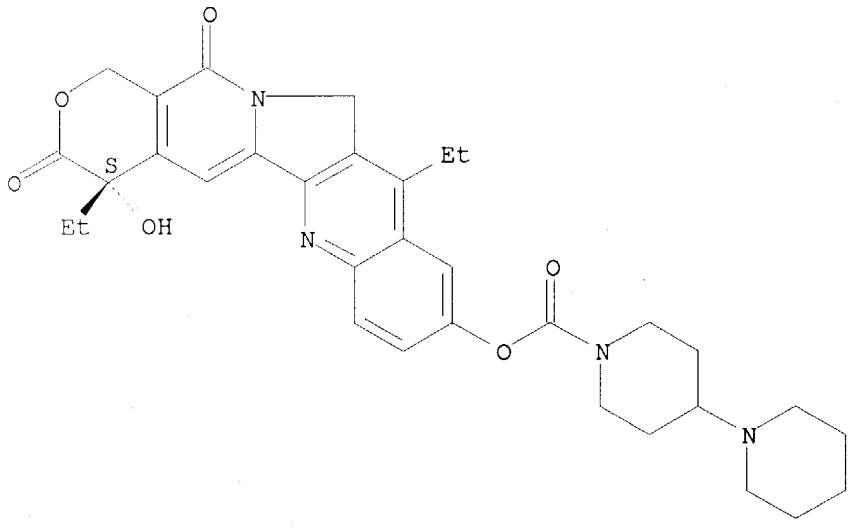
IT 50-18-0, Cyclophosphamide 51-21-8, Fluorouracil 52-24-4, Thiotepa 53-86-1, Indomethacin 57-22-7, Vincristine 58-05-9, Leucovorin 76-43-7, Fluoxymesterone 128-13-2, Ursodeoxycholic acid 302-79-4, Retinoic acid 471-34-1, Calcium carbonate, biological studies 865-21-4, Vinblastine 1464-42-2, Selenomethionine 3562-63-8, Megestrol 7782-49-2, Selenium, biological studies 10540-29-1, Tamoxifen 14769-73-4, Levamisole 15663-27-1, Cisplatin 15866-90-7 23214-92-8, Doxorubicin 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin 51803-78-2 59973-80-7, Sulindac sulfone 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 65807-02-5, Goserelin 70052-12-9, Eflornithine 71486-22-1, Vinorelbine 80937-31-1 84449-90-1, Raloxifene 89778-26-7, Toremifene 93014-16-5 95058-81-4, Gemcitabine **97682-44-5**, Irinotecan 107868-30-4, Exemestane 112809-51-5, Letrozole 114977-28-5, Docetaxel 120511-73-1, Anastrozole 123653-11-2 123663-49-0 123948-87-8, Topotecan 154039-60-8 154361-50-9, Capecitabine 158205-05-1 158959-32-1 162011-90-7, Rofecoxib 162054-19-5 **169590-42-5**, Celecoxib 170569-86-5 170569-87-6 170569-88-7 170630-40-7 177660-77-4 177660-95-6 178816-61-0 178816-94-9, [1,1':2',1''-Terphenyl]-4-sulfonamide 179382-91-3 179545-77-8 180200-68-4, JTE-522 181485-41-6 181695-72-7, Valdecoxib 181695-81-8 181696-33-3 187845-71-2 187845-80-3 189954-13-0 189954-16-3 191537-76-5 192329-42-3 197239-97-7 197239-99-9 197240-09-8 197240-14-5 197904-84-0 197905-01-4 198470-84-7 212126-32-4 215123-80-1 226388-60-9 226388-66-5 226389-91-9 226395-57-9 226395-66-0 226395-67-1

226395-93-3 226396-02-7 226396-03-8 226396-26-5 226703-01-1
227619-96-7 251972-30-2, SC-58236 279221-12-4 279221-13-5
279221-14-6 279221-15-7 279221-16-8 279221-17-9 279221-18-0
279221-19-1 279221-20-4 279221-21-5 279221-22-6 279221-23-7
279221-24-8 279221-25-9 279221-26-0 279221-27-1 279221-28-2
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

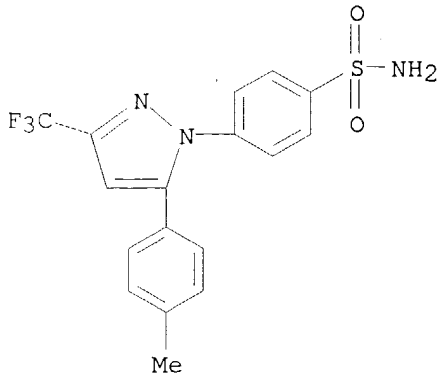
IT **97682-44-5**, Irinotecan **169590-42-5**, Celecoxib
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for neoplasia treatment)

RN 97682-44-5 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)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N
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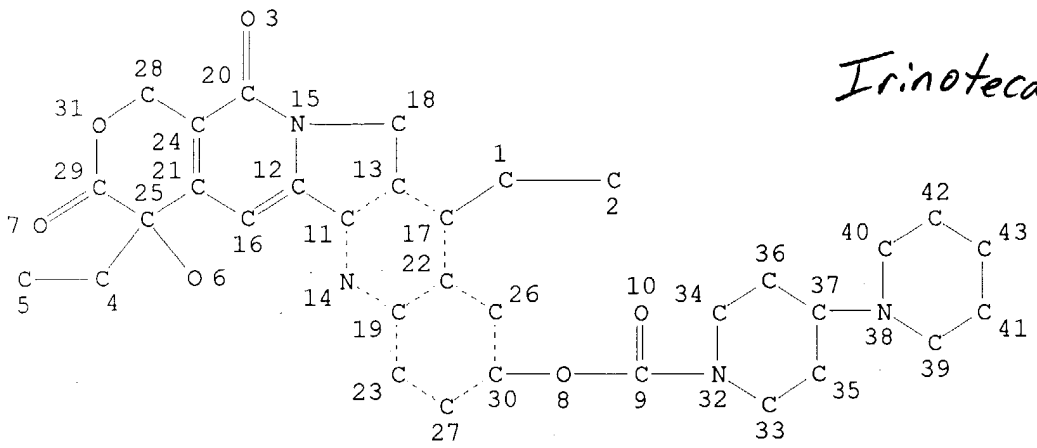
L2 STR



Irinotecan as antineoplastic

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 43

STEREO ATTRIBUTES: NONE
L3 10 SEA FILE=REGISTRY FAM FUL L2
L7 1080 SEA FILE=HCAPLUS ABB=ON PLU=ON L3(L)(BAC OR DMA OR PAC OR PKT OR THU)/RL
L16 708 SEA FILE=HCAPLUS ABB=ON PLU=ON L3(L)(CANCER? OR ANTINEOPLAS? OR NEOPLAS? OR TUMOR? OR ANTITUMOR)
L18 660 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 AND L7

=> d l18 ibib ab hitstr 1-5 650-660 ← only selected references of the 660 printed

L18 ANSWER 1 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:934743 HCAPLUS
TITLE: CPT-11 and cisplatin in the treatment of advanced gastric cancer in Asians
AUTHOR(S): Lim, W.-T.; Lim, S.-T.; Wong, N.-S.; Koo, W.-H.
CORPORATE SOURCE: Department of Medical Oncology, National Cancer Centre Singapore, Singapore
SOURCE: Journal of Chemotherapy (Firenze, Italy) (2003), 15(4), 400-405
CODEN: JCHEEU; ISSN: 1120-009X
PUBLISHER: E.I.F.T. srl
DOCUMENT TYPE: Journal
LANGUAGE: English
AB There is no std. chemotherapy for advanced gastric cancer. A combination of CPT-11 and cisplatin was evaluated for response and toxicity in Asians. 38 Patients with histol. proven stage IV gastric/gastroesophageal junction adenocarcinoma were treated with CPT-11 50 mg/m2 and cisplatin 30 mg/m2

weekly for 3 wk. Each cycle was repeated every 28 days. The median no. of cycles was 1.66 (range 0.33-4.33). Dose delay was needed in 11 (29%) patients and dose redns. in 19 (50%) patients. The overall response rate was 42%. There was no complete response. Grade 3 and 4 hematol. toxicity was 26%. Grade 3 or 4 diarrhea was not common. Median time to progression for all patients was 15 wk. Median duration of survival of all patients was 42 wk. Patients with better performance status and no prior chemotherapy did better. CPT-11 and cisplatin is a useful regimen with significant but manageable toxicity that can be administered without a central venous catheter.

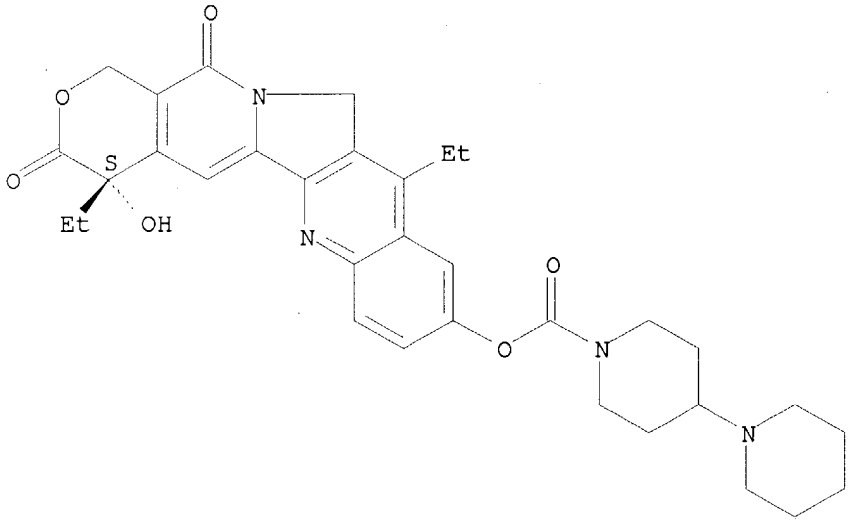
IT **100286-90-6**, CPT-11
RL: ADV (Adverse effect, including toxicity); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(efficacy of CPT-11 and cisplatin in treatment of advanced gastric **cancer**)

RN 100286-90-6 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A

● HCl

L18 ANSWER 2 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:931412 HCAPLUS
DOCUMENT NUMBER: 139:375004
TITLE: Treatment of cancer by the use of anti Fas antibody
INVENTOR(S): Johnston, Patrick; Longley, Daniel

PATENT ASSIGNEE(S): Fusion Antibodies Limited, UK
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097698	A1	20031127	WO 2003-GB2109	20030516

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

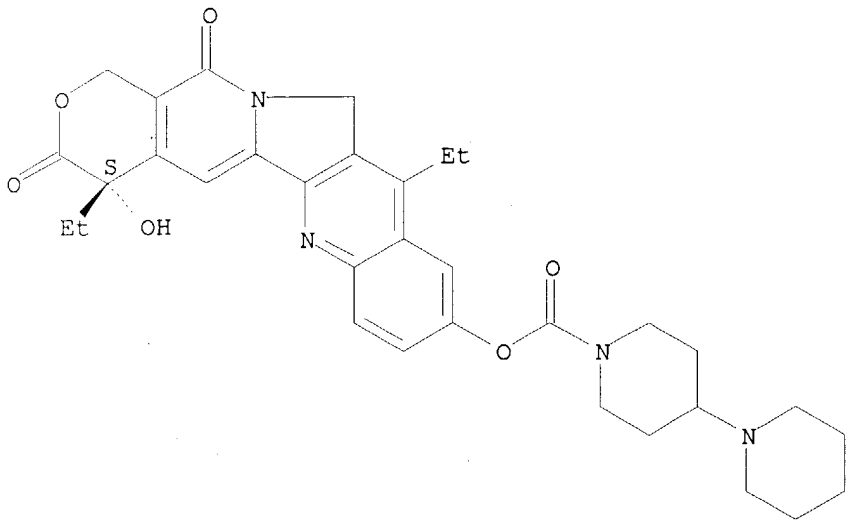
PRIORITY APPLN. INFO.: GB 2002-11377 A 20020517
GB 2002-14885 A 20020627

AB The present invention provides a method of killing cancer cells and method of treatment of cancer comprising administration of a therapeutically effective amt. of (a) a specific binding member which binds to a cell death receptor or a nucleic acid encoding said binding member and (b) a chemotherapeutic agent. The binding member preferably binds to a Fas receptor, and is preferably an antibody. Also described are medicaments for use in treating cancer.

IT **97682-44-5**, Irinotecan
RL: **PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(Fas antibody and chemotherapeutic agents in **cancer** treatment)

RN 97682-44-5 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:931176 HCAPLUS
TITLE: Methods and compositions using immunomodulatory compounds for treatment and management of cancers and other diseases
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097052	A2	20031127	WO 2003-US15470	20030516

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-380842P P 20020517
US 2002-424600P P 20021106

AB Methods of treating, preventing and/or managing cancer as well as and diseases and disorders assocd. with, or characterized by, undesired angiogenesis are disclosed. Specific methods encompass the administration of an immunomodulatory compd. alone or in combination with a second active

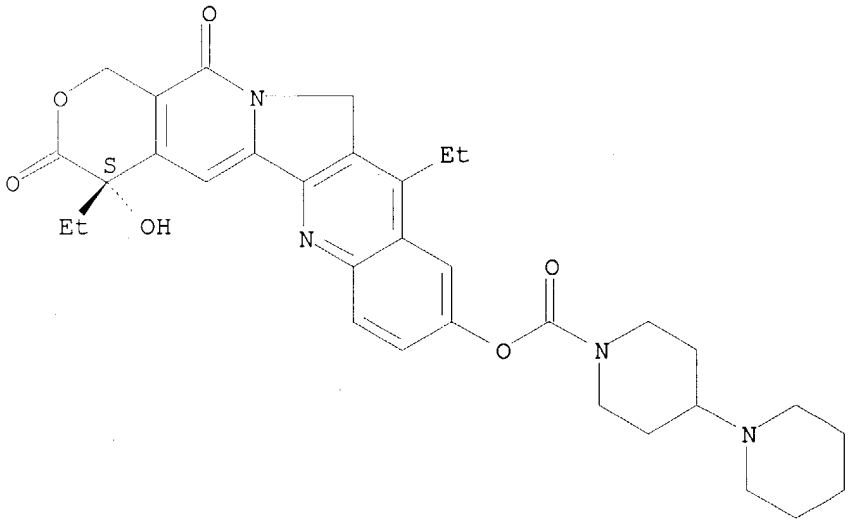
ingredient. The invention further relates to methods of reducing or avoiding adverse side effects assocd. with chemotherapy, radiation therapy, hormonal therapy, biol. therapy or immunotherapy which comprise the administration of an immunomodulatory compd. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

IT **97682-44-5**, Irinotecan
RL: **PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods and compns. using immunomodulatory compds. for treatment and management of **cancers** and other diseases in combination with other agents)

RN 97682-44-5 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L18 ANSWER 4 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:931165 HCAPLUS
TITLE: Methods and compositions using selective cytokine inhibitory drugs for treatment and management of cancers and other diseases
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097040	A1	20031127	WO 2003-US15468	20030516

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-380842P P 20020517
US 2002-424601P P 20021106

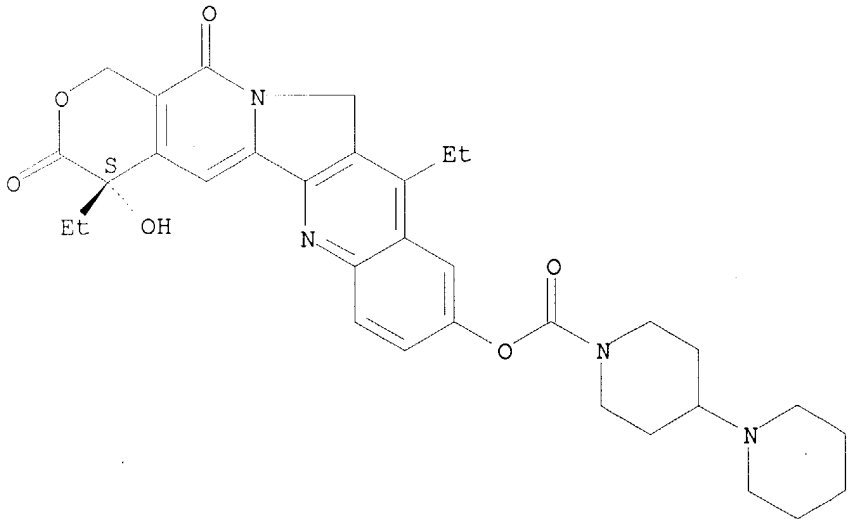
AB Methods of treating, preventing and/or managing cancer as well as and diseases and disorders assocd. with, or characterized by, undesired angiogenesis are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug alone or in combination with a second active ingredient. The invention further relates to methods of reducing or avoiding adverse side effects assocd. with chemotherapy, radiation therapy, hormonal therapy, biol. therapy or immunotherapy which comprise the administration of a selective cytokine inhibitory drug. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

IT **97682-44-5**, Irinotecan
RL: **PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods and compns. using selective cytokine inhibitory drugs for treatment and management of **cancers** and other diseases)

RN 97682-44-5 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:922835 HCAPLUS
TITLE: Progress in the medical treatment of advanced colorectal cancer
AUTHOR(S): Fabre-Guillevin, Elizabeth; Piedbois, Pascal; Buyse, Marc
CORPORATE SOURCE: Department of Medical Oncology, Henri Mondor Hospital, Creteil, 94000, Fr.
SOURCE: Expert Review of Anticancer Therapy (2003), 3(5), 711-716
CODEN: ERATBJ; ISSN: 1473-7140
PUBLISHER: Future Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

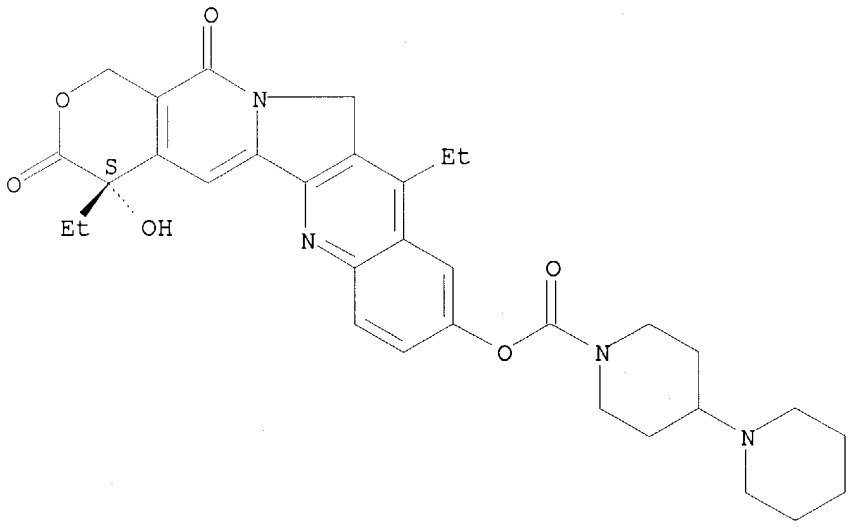
AB A review. Despite recent progress made in screening, prevention and adjuvant treatment of colorectal cancer, a large proportion of patients with this disease develop local recurrences or distant metastases. The management of these patients requires a multidisciplinary approach. Surgery must be performed whenever possible for metastases confined to the liver or lung. However, in most cases, chemotherapy and supportive care are the only feasible treatments. This review describes the research carried out in this field through randomized trials and meta-analyses aimed at optimizing the efficacy of front-line chemotherapy.

IT **100286-90-6**, Campto
RL: **PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(treatment options for advanced colorectal **cancer**)

RN 100286-90-6 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



● HCl

L18 ANSWER 650 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:187631 HCAPLUS
DOCUMENT NUMBER: 116:187631
TITLE: Effects of CPT-11 in combination with other anti-cancer agents in culture
AUTHOR(S): Kano, Yasuhiko; Suzuki, Kenichi; Akutsu, Miyuki; Suda, Keiichi; Inoue, Yoshiharu; Yoshida, Minoru; Sakamoto, Shinobu; Miura, Yasusada
CORPORATE SOURCE: Div. Med. Oncol., Tochigi Cancer Cent., Utsunomiya, 320, Japan
SOURCE: International Journal of Cancer (1992), 50(4), 604-10
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English

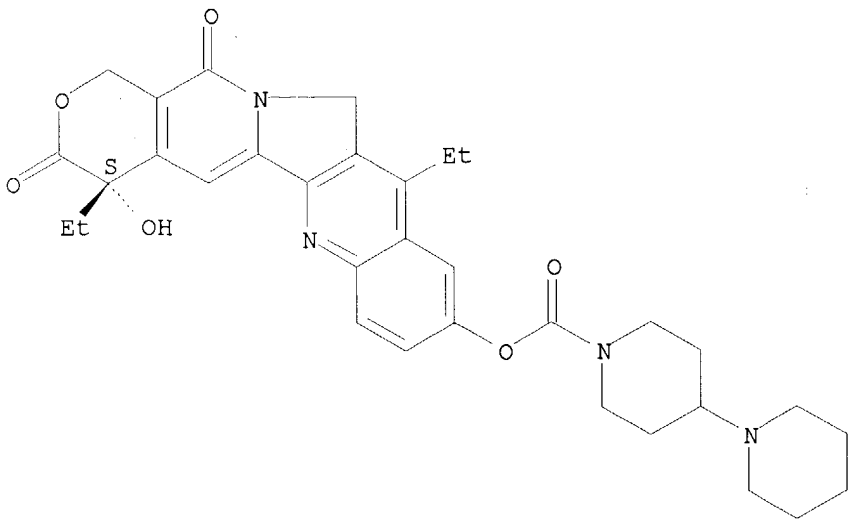
AB CPT-11 [7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxycamptothecin] is a water-sol. antitumor deriv. undergoing phase-II evaluation. The effects of CPT-11 in combination with 11 other anticancer agents were studied on the human T-cell leukemia cell line MOLT-3 in culture. Both CPT-11 and SN-38 (active substance of CPT-11 in vivo) were used. Cells were incubated for 3 days in the presence of 2 drugs (CPT-11 or SN-38 and another drug) and cytotoxic effects were detd. Supra-additive and marginally supra-additive effects (synergism) were obsd. for CPT-11 in combination with cisplatin, cytosine arabinoside, and mitomycin C. Additive effects were obsd. for the combinations with amsacrine, bleomycin, doxorubicin, etoposide, 5-fluorouracil, mitoxantrone, and vincristine. Alternate subadditive and cytoprotective effects (antagonism) were obsd. for CPT-11 in combination with methotrexate. Similar tendencies were obsd. for SN-38 in combination with other agents. Thus, CPT-11 in the presence of anticancer agents produces synergistic cytotoxicity. Of these agents, cisplatin, cytosine arabinoside, and mitomycin C are most suitable for simultaneous administration with CPT-11.

IT **100286-90-6**, CPT 11
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**neoplasm** inhibition by, other drugs synergism with)

RN 100286-90-6 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A

● HCl

L18 ANSWER 651 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:51031 HCAPLUS
DOCUMENT NUMBER: 116:51031
TITLE: Augmentation of the antiproliferative activity of CPT-11, a new derivative of camptothecin, by tumor necrosis factor against proliferation of gynecologic tumor cell lines
AUTHOR(S): Mori, Hidehiro; Sawairi, Miho; Itoh, Naoki; Hanabayashi, Takahiro; Kondoh, Hideaki; Tamaya, Teruhiko
CORPORATE SOURCE: Sch. Med., Gifu Univ., Gifu, 500, Japan
SOURCE: Anti-Cancer Drugs (1991), 2(5), 469-74
CODEN: ANTDEV; ISSN: 0959-4973
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The cooperative effects of recombinant human tumor necrosis factor (rH-TNF) and CPT-11 (I), a new deriv. of camptothecin, against the proliferation of human gynecol. tumor cell lines were examd. in vitro. The Ishikawa cells were responsive to rH-TNF, the HHUA cells exhibited a minimal degree of responsiveness to rH-TNF, and the HeLa S3 and Caov-3 cells were unresponsive to rH-TNF. The HHUA, Ishikawa and Caov-3 cells were responsive to CPT-11, and the HeLa S3 cells were relatively sensitive to CPT-11 cytotoxicity. In all 4 cell lines, rH-TNF at clin. achievable concns. exhibited synergy with CPT-11. The combination therapy of rH-TNF and CPT-11 will be a new approach against gynecol. cancers.

IT **100286-90-6**, CPT-11
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)

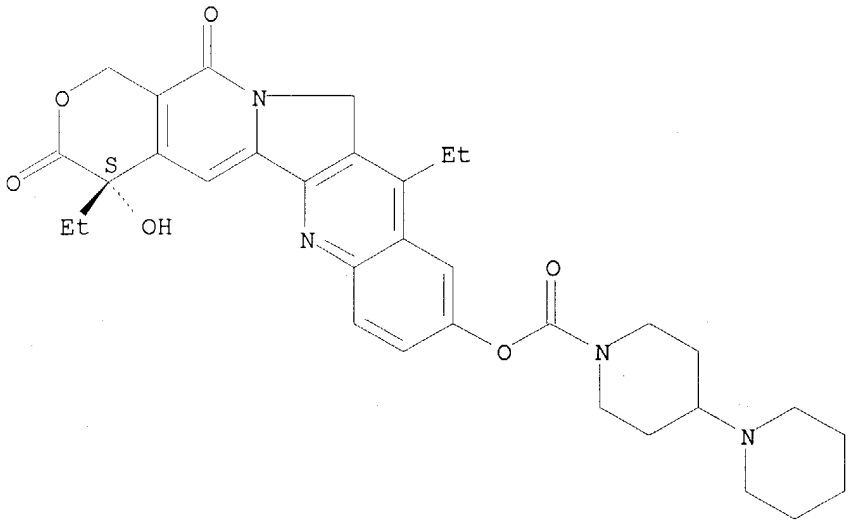
(**antitumor** activity of **tumor** necrosis factor combination with, in gynecol. **tumor** cell lines)

RN 100286-90-6 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A

● HCl

L18 ANSWER 652 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1992:34049 HCAPLUS

DOCUMENT NUMBER: 116:34049

TITLE: DNA topoisomerase inhibitor as chemotherapeutic drug. Clinical point of view

AUTHOR(S): Taguchi, Tetsuo

CORPORATE SOURCE: Research Inst. Microb. Dis., Osaka Univ., Suita, 565, Japan

SOURCE: Gan to Kagaku Ryoho (1991), 18(10), 1574-8
CODEN: GTKRDX; ISSN: 0385-0684

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

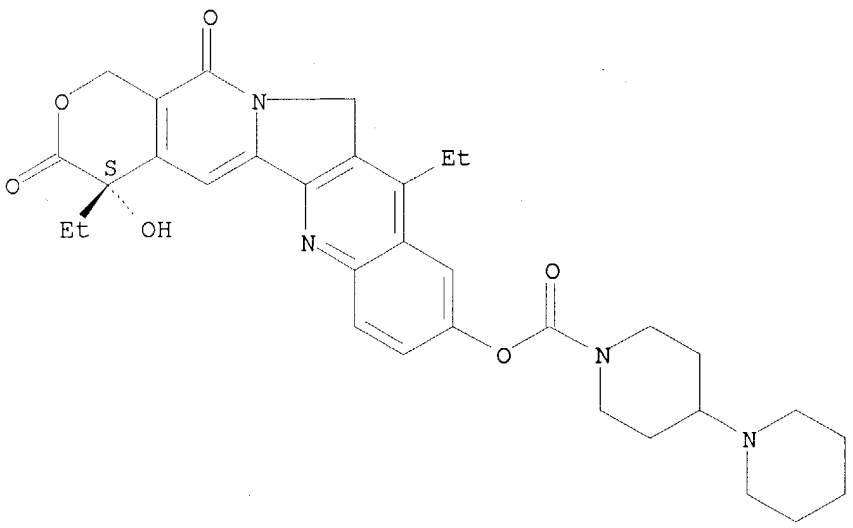
AB Pharmacol. and chem. studies of the antitumor DNA topoisomerase I inhibitor, CPT-11 (I) are reported.

IT **100286-90-6**, CPT-11
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**antitumor** activity of, as DNA topoisomerase I inhibitor)

RN 100286-90-6 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A

● HCl

L18 ANSWER 653 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:597871 HCAPLUS
DOCUMENT NUMBER: 115:197871
TITLE: Antitumor activity of a camptothecin derivative, CPT-11, against human tumor xenografts in nude mice
AUTHOR(S): Kawato, Yasuyoshi; Furuta, Tomio; Aonuma, Masashi; Yasuoka, Megumi; Yokokura, Teruo; Matsumoto, Kensuke
CORPORATE SOURCE: Explor. Res. Lab., Daiichi Pharm. Co., Ltd., Tokyo, 134, Japan
SOURCE: Cancer Chemotherapy and Pharmacology (1991), 28(3), 192-8
CODEN: CCPHDZ; ISSN: 0344-5704
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antitumor effects of the camptothecin (CPT) deriv. CPT-11 (I) were tested on human tumor xenografts in nude mice. CPT-11 showed antitumor activity higher than that of Adriamycin, 5-fluroruracil, or futraful, with little or no redn. of body wt. being obsd. in the mice. The growth of colon adenocarcinoma Co-4 was significantly inhibited after a single i.v. injection of CPT-11 at 25, 50, or 100 mg/kg. The single i.v. injection was also significantly effective against mammary carcinoma MX-1 and

gastric adenocarcinoma St-15. All of the mice bearing MX-1 tumors were cured by the administration of CPT-11 every 4 days for a total of three treatments at a total dose of 100 mg/kg given i.v. or of 400 mg/kg given p.o. Three i.v. or oral treatments were also effective against Co-4, St-15, gastric adenocarcinoma SC-6, and squamous-cell lung carcinoma QG-56. To achieve the same efficacy attained by i.v. injection, however, oral doses 2-4 times higher than the i.v. doses were required. When the total dose was fixed at 100 mg/kg, a triple i.v. injection was most effective, followed by a single i.v. injection and, finally daily p.o. administration for 10 days. Although SN-38 (II) a metabolite of CPT-11, showed much stronger cytotoxic activity in vitro than did CPT-11, its antitumor effects were similar, if not inferior, to those of CPT-11 in vivo at the same dose level. CPT-11 was converted into SN-38 by human tumors, but the sensitivity of these tumors to CPT-11 in vivo was independent of their ability to produce SN-38. These results suggest that CPT-11 may be clin. effective, depending on the schedule of administration, but that its effectiveness is not related to the ability of the tumor to produce SN-38.

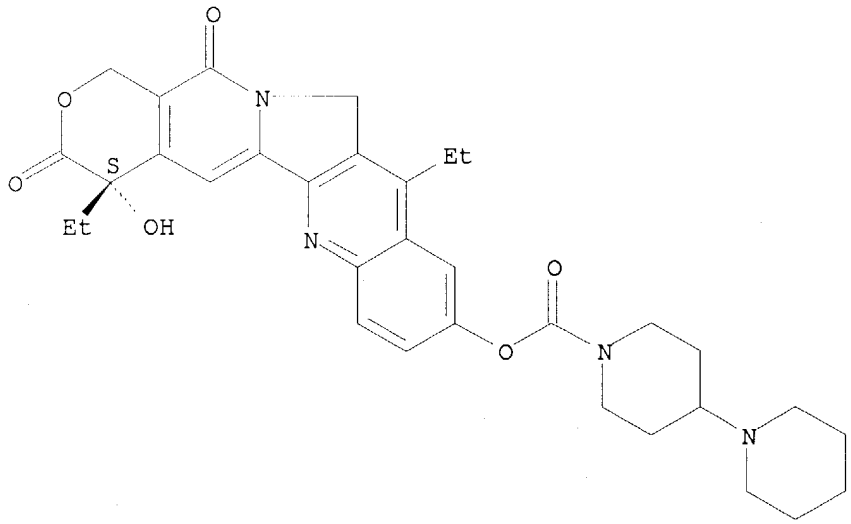
IT **100286-90-6**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**antitumor** activity of)

RN 100286-90-6 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A

● HCl

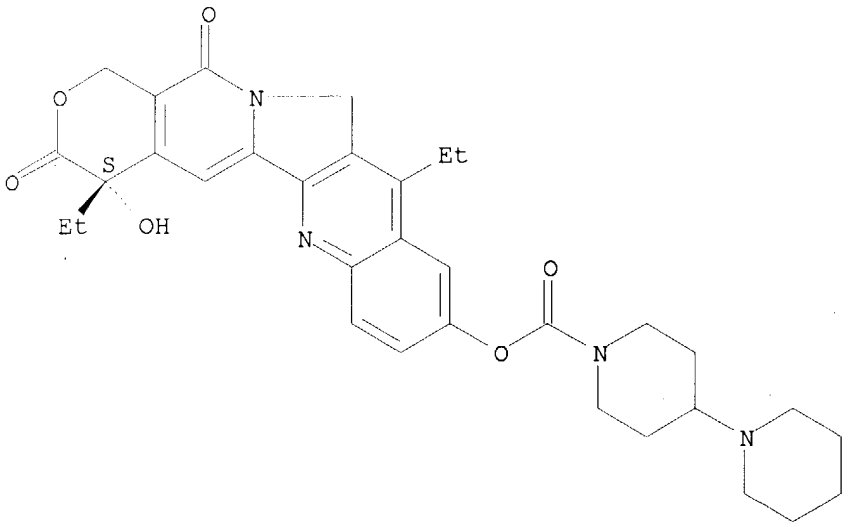
L18 ANSWER 654 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:583643 HCAPLUS
DOCUMENT NUMBER: 115:183643
TITLE: Synthesis and antitumor activity of 20(S)-camptothecin derivatives: carbamate-linked, water-soluble derivatives of 7-ethyl-10-hydroxycamptothecin
AUTHOR(S): Sawada, Seigo; Okajima, Satoru; Aiyama, Ritsuo; Nokata, Kenichiro; Furuta, Tomio; Yokokura, Teruo; Sugino, Eiichi; Yamaguchi, Kentaro; Miyasaka, Tadashi
CORPORATE SOURCE: Yakult Inst. Microbiol. Res., Kunitachi, 186, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1991), 39(6), 1446-54
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Novel 36 derivs. bonding the phenolic hydroxyl group of 7-ethyl-10-hydroxycamptothecin with diamines through a monocarbamate linkage, e.g. I (R = lower alkyl, R1 = Me2NCH2CH2, Et2NCH2CH2, RR1N = substituted piperazino, aminopiperidino) were synthesized and their antitumor activity was evaluated in vivo. The derivs. were sol. in water as their HCl salts with the E lactone ring intact and exhibited significant antitumor activity. I (RR1N = 4-piperidinopiperidino) showed excellent activity against L1210 leukemia and other murine tumors. The structure of its hydrochloride trihydrate was detd. by spectroscopic and crystallog. methods.

IT **97682-44-5P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and **antitumor** activity of)

RN 97682-44-5 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L18 ANSWER 655 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:549885 HCAPLUS
DOCUMENT NUMBER: 115:149885
TITLE: Intracellular roles of SN-38, a metabolite of the camptothecin derivative CPT-11, in the antitumor effect of CPT-11
AUTHOR(S): Kawato, Yasuyoshi; Aonuma, Masashi; Hirota, Yasuhide; Kuga, Hiroshi; Sato, Keiko
CORPORATE SOURCE: Explor. Res. Lab. 1, Daiichi Pharm. Co., Ltd., Tokyo, 134, Japan
SOURCE: Cancer Research (1991), 51(16), 4187-91
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English

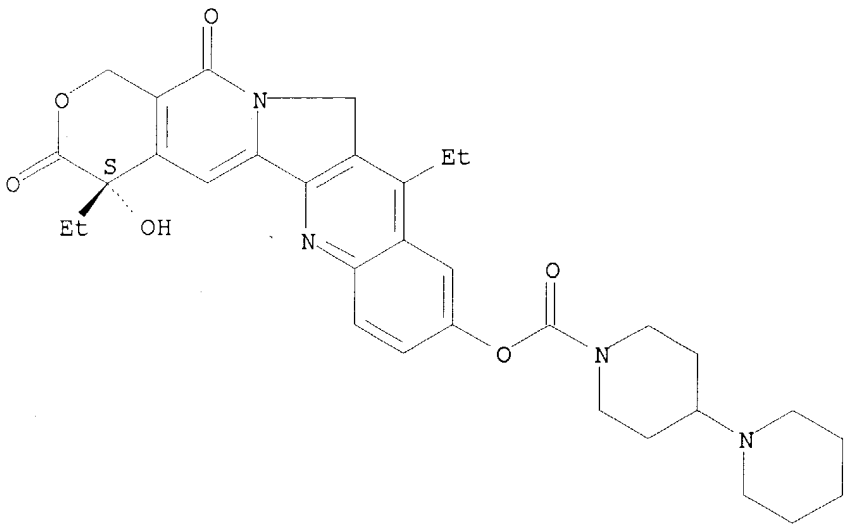
AB It is known that 7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxycamptothecin (CPT-11), a semisynthesized deriv. of camptothecin (CPT), has a potent antitumor activity in vivo, but 7-ethyl-10-hydroxycamptothecin (SN-38), a metabolite of CPT-11, shows much stronger cytotoxicity in vitro than CPT-11. In this study, it is demonstrated that the relaxation of SV40 DNA plasmids by type I DNA topoisomerase prepd. from P388 murine leukemia cells was inhibited 50% by SN-38 at approx. 1 .mu.M, although CPT-11 at 1 mM slightly inhibited the relaxation. SN-38 and CPT showed strong, time-dependent inhibitory activity against DNA synthesis of P388 cells. However, CPT-11 weakly inhibited DNA synthesis independently of time with coincident inhibition of the total thymidine uptake by the cells. By alk. and neutral elution assays, it was demonstrated that SN-38 caused much more frequent DNA single-strand breaks in P388 cells than did CPT-11. The same content of SN-38 and a similar frequency of single-strand breaks were detected in the cells treated with SN-38 at 0.1 .mu.M or with CPT-11 at 100 .mu.M. Therefore, single-strand breaks by CPT-11 seem to be due to SN-38 produced from CPT-11 in cells. These results indicate that CPT-11 itself possesses a marginal antiproliferative effect but that SN-38 plays an essential role in the mechanism of action of CPT-11.

IT **100286-90-6**, CPT-11
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**neoplasm**-inhibiting activity of, mechanism of, metabolite in)

RN 100286-90-6 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A

● HCl

L18 ANSWER 656 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:43274 HCAPLUS
DOCUMENT NUMBER: 114:43274
TITLE: Synthesis of water-soluble (aminoalkyl)camptothecin analogs: inhibition of topoisomerase I and antitumor activity
AUTHOR(S): Kingsbury, William D.; Boehm, Jeffrey C.; Jakas, Dalia R.; Holden, Kenneth G.; Hecht, Sidney M.; Gallagher, Gregory; Caranfa, Mary Jo; McCabe, Francis L.; Faucette, Leo F.; et al.
CORPORATE SOURCE: Dep. Med. Chem., SmithKline Beecham Pharm., King of Prussia, PA, 19406, USA
SOURCE: Journal of Medicinal Chemistry (1991), 34(1), 98-107
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:43274

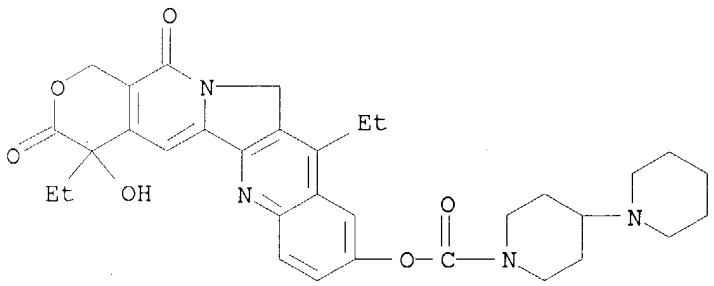
AB Water-sol. analogs of the antitumor alkaloid camptothecin were prepd. in which aminoalkyl groups were introduced into ring A or B. Most of the analogs were prepd. by oxidn. of camptothecin to 10-hydroxycamptothecin (I) followed by a Mannich reaction to give N-substituted 9-(aminomethyl)-10-hydroxycamptothecins or by subsequent modification of Mannich product II. Others were obtained by modification of the hydroxyl group of I or by total synthesis. These analogs, as well as some of their synthetic precursors, were evaluated for inhibition of topoisomerase I, cytotoxicity, and antitumor activity. Although there was not a quant. correlation between these assays, compds. that inhibited topoisomerase I were also cytotoxic and demonstrated antitumor activity in vivo. Further

evaluation of the most active water-sol. analog led to the selection of II for development as an antitumor agent. In addn. to its water soly., ease of synthesis from natural camptothecin, and high potency, II demonstrated broad-spectrum activity in preclin. tumor models and is currently undergoing Phase I clin. trials in cancer patients.

IT **130144-33-1P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and **antitumor** activity of)

RN 130144-33-1 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, 4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester (9CI) (CA INDEX NAME)



L18 ANSWER 657 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1990:210658 HCAPLUS

DOCUMENT NUMBER: 112:210658

TITLE: Effect of administration schedules on the antitumor activity of CPT-11, a camptothecin derivative

AUTHOR(S): Furuta, Tomio; Yokokura, Teruo

CORPORATE SOURCE: Yakult Cent. Inst. Microbiol. Res., Japan

SOURCE: Gan to Kagaku Ryoho (1990), 17(1), 121-30
CODEN: GTKRDX; ISSN: 0385-0684

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB The effect of administration schedules on the antitumor activity of CPT-11, a novel deriv. of camptothecin, against mouse L 1210 leukemia and Meth A fibrosarcoma was investigated. At the same total dose, CPT-11 showed more significant antitumor activity after repeated administration. The most effective administration intervals were 5 days for L 1210 and 1 to 3 days for Meth A. CPT-11 showed a considerable antitumor activity by the repeated treatments for 2 or 3 times of continuous administration for 3 to 5 days.

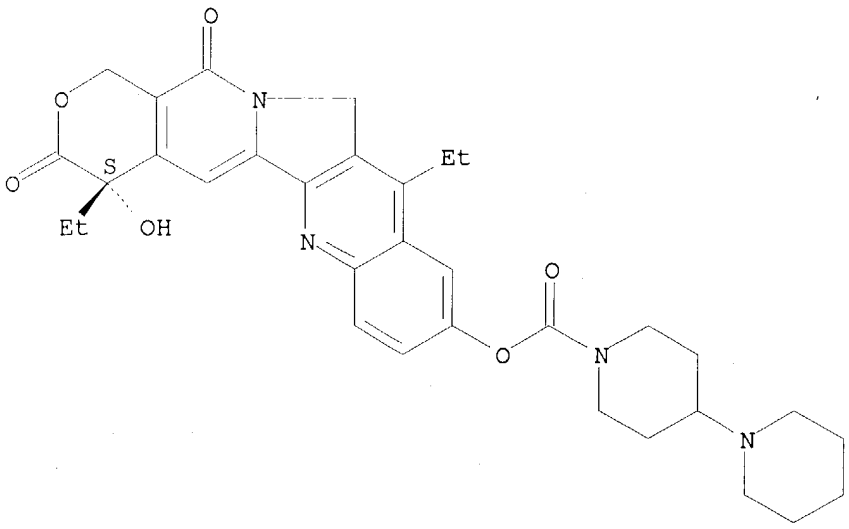
IT **100286-90-6**, CPT 11
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**antitumor** activity of)

RN 100286-90-6 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A

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L18 ANSWER 658 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1988:197945 HCAPLUS
DOCUMENT NUMBER: 108:197945
TITLE: Antitumor effect of CPT-11, a new derivative of camptothecin, against pleiotropic drug-resistant tumors in vitro and in vivo
AUTHOR(S): Tsuruo, Takashi; Matsuzaki, Takeshi; Matsushita, Miyuki; Saito, Harumi; Yokokura, Teruo
CORPORATE SOURCE: Cancer Chemother. Cent., Jap. Found. Cancer Res., Toshima, Japan
SOURCE: Cancer Chemotherapy and Pharmacology (1988), 21(1), 71-4
CODEN: CCPHDZ; ISSN: 0344-5704
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CPT-11 (I), a new deriv. of camptothecin, was effective against tumor cells, esp. vincristine (VCR)- and adriamycin (ADM)-resistant P388 leukemia, compared to either VCR or ADM. The drug showed superior chemotherapeutic effects over VCR and ADM in sensitive P388 leukemia-bearing mice, and was also effective in VCR- and ADM-resistant P388 leukemia-bearing mice. These latter survival and advantages with CPT-11 were almost equal to those obtained by CPT-11 against sensitive P388 leukemia. CPT-11 was effective against human tumor cells, esp. various pleiotropically drug-resistant human tumor lines, compared to VCR and ADM. CPT-11 should be considered for further development as a new

chemotherapeutic agent potentially effective against pleiotropically drug-resistant tumors.

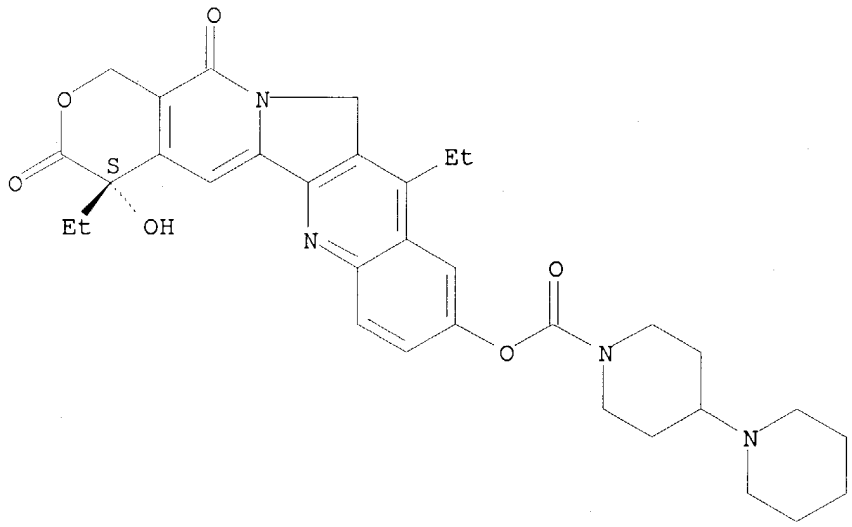
IT **100286-90-6**, CPT-11
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**antitumor** activity of)

RN 100286-90-6 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A

● HCl

L18 ANSWER 659 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1988:197908 HCAPLUS

DOCUMENT NUMBER: 108:197908

TITLE: Antitumor activity of 7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxycamptothecin, a novel water-soluble derivative of camptothecin, against murine tumors

AUTHOR(S): Kunimoto, Takehiko; Nitta, Kazuo; Tanaka, Tomiko; Uehara, Nobuaki; Baba, Hiroyasu; Takeuchi, Mieko; Yokokura, Teruo; Sawada, Siego; Miyasaka, Tadashi; Mutai, Masahiko

CORPORATE SOURCE: Chemother. Div., Natl. Cancer Cent. Res. Inst., Tokyo, 104, Japan

SOURCE: Cancer Research (1987), 47(22), 5944-7

CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The search for new water-sol. analogs of camptothecin (CPT) with higher activity and less toxicity has led to the development of a novel compd., 7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxycamptothecin (CPT-11) (I) which had antitumor activity against a broad spectrum of exptl. tumor models by i.p., i.v., or oral administration. CPT-11 was more active than CPT and some of its known derivs. and produced higher max. increase in life span (ILS) with good activity over a wide dose range. against L1210. CPT-11 was actve against both ascites and solid tumors; the more susceptible murine tumors were S180, Meth A fibrosarcoma, Lewis lung carcinoma, Ehrlich carcinoma, MH134 hepatoma, mammary carcinoma of C3H/HeN mice, L1210, and P388 leukemia. The antitumor activity of CPT-11 against i.p. implanted L1210 was superior to that of adriamycin. The acute toxicity of CPT-11 was very low, particularly when administerd orally.

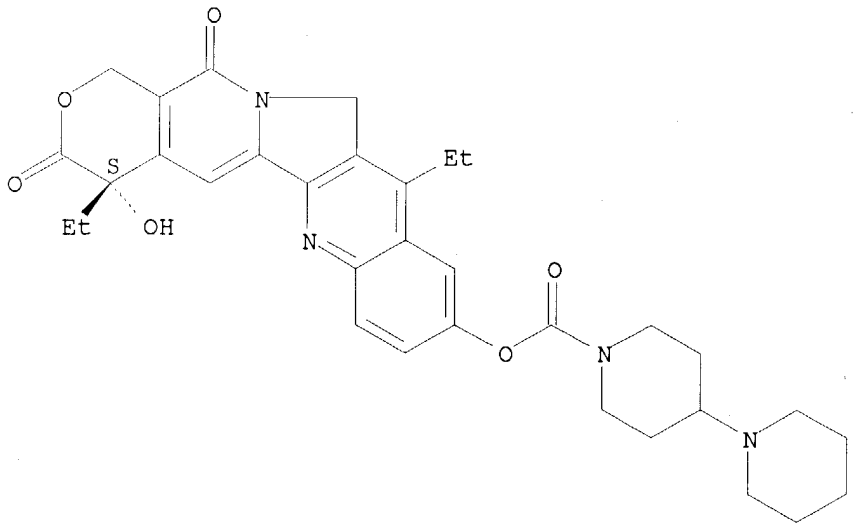
IT **100286-90-6**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**neoplasm** inhibition by)

RN 100286-90-6 HCAPLUS

CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A

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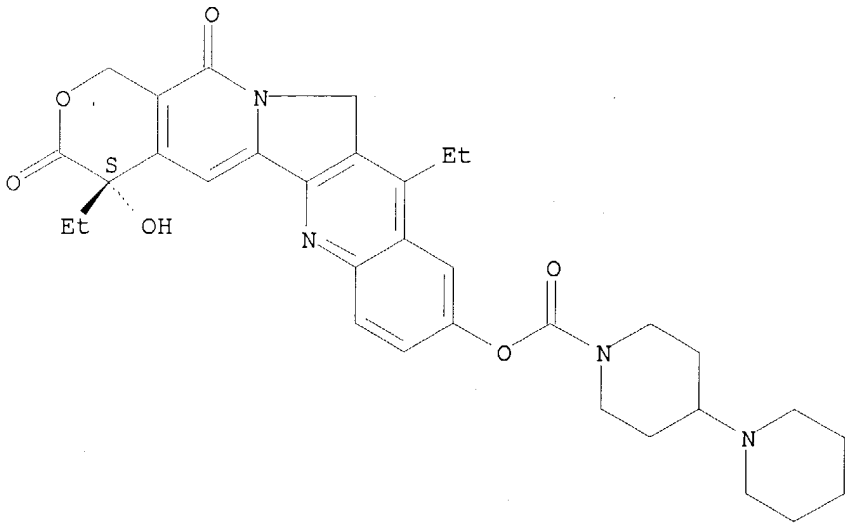
L18 ANSWER 660 OF 660 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1986:618440 HCAPLUS
DOCUMENT NUMBER: 105:218440
TITLE: Antitumor activity of a new derivative of camptothecin
AUTHOR(S): Nitta, K.; Yokokura, T.; Sawada, S.; Takeuchi, M.; Tanaka, T.; Uehara, N.; Baba, H.; Kunimoto, T.; Miyasaka, T.; Mutai, M.
CORPORATE SOURCE: Chemother. Div., Natl. Cancer Cent. Res. Inst., Tokyo, Japan
SOURCE: Recent Adv. Chemother., Proc. Int. Congr. Chemother., 14th (1985), Volume Anticancer Sect. 1, 28-30. Editor(s): Ishigami, Joji. Univ. Tokyo Press: Tokyo, Japan.
CODEN: 55GNAX
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Among the many derivs. of camptothecin which were prepd., CPT-11 (I) [**100286-90-6**] showed strong **antitumor** activity against various kinds of murine **tumors**, both in ascites and in solid forms, after i.p., i.v., or oral administration. When administered i.p., CPT-11 was very effective against ascites forms of S180, Ehrlich **cancer**, MH134, Meth A, L1210 and P388 and solid forms of Lewis lung and Ehrlich **cancers**. It was also effective against the ascites form of B16 and the solid form of MH134 and syngeneic mammary carcinoma. Oral treatment with CPT-11 showed strong **antitumor** activity, although the efficiency was lower than with i.p. treatment.
IT **100286-90-6P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and **neoplasm**-inhibiting activity of)
RN 100286-90-6 HCAPLUS
CN [1,4'-Bipiperidine]-1'-carboxylic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



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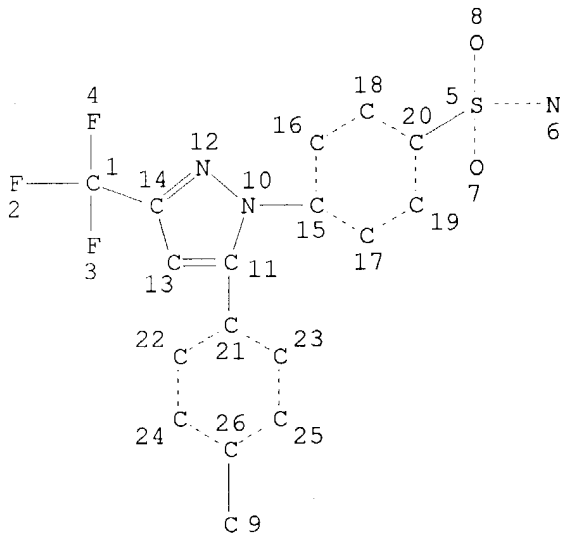


Celecoxib as antineoplastic

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
L6 26 SEA FILE=REGISTRY FAM FUL L5
L8 665 SEA FILE=HCAPLUS ABB=ON PLU=ON L6(L)(BAC OR DMA OR PAC OR PKT OR THU)/RL
L17 79 SEA FILE=HCAPLUS ABB=ON PLU=ON L6(L)(CANCER? OR ANTINEOPLAS? OR NEOPLAS? OR TUMOR? OR ANTITUMOR)
L19 77 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND L8

=> d l19 ibib ab hitstr 1-5 67-77 — only selected references printed.

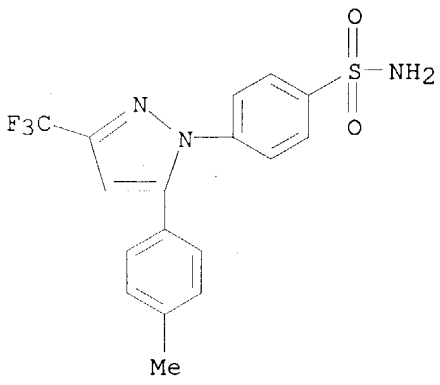
L19 ANSWER 1 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:919948 HCAPLUS
TITLE: Use of NSAIDs for the chemoprevention of colorectal cancer
AUTHOR(S): Herendeen, Jill M.; Lindley, Celeste
CORPORATE SOURCE: Drug Development Fellow, University of North Carolina School of Pharmacy, Chapel Hill, NC, USA
SOURCE: Annals of Pharmacotherapy (2003), 37(11), 1664-1674
CODEN: APHRER; ISSN: 1060-0280
PUBLISHER: Harvey Whitney Books Co.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. OBJECTIVE: To discuss the role of nonsteroidal antiinflammatory drugs (NSAIDs) in the chemoprevention of colorectal cancer. DATA SOURCES:

A MEDLINE search (1966-May 2003) was performed to identify key literature. Search items included, but were not limited to, NSAIDs, colorectal cancer, chemoprevention, cyclooxygenase-2 (COX-2)-specific inhibitors, and familial adenomatous polyposis (FAP). STUDY SELECTION AND DATA Extn.: The search included exptl. (in vitro and animal models) and clin. studies evaluating the use of NSAIDs for the chemoprevention of colorectal cancer. The MEDLINE search was supplemented by refs. from selected articles. DATA SYNTHESIS: Numerous exptl., epidemiol., and clin. studies suggest that NSAIDs have promise as anticancer agents. The mechanism by which NSAIDs lead to decreased colon carcinogenesis is not fully understood, but may involve restoration of apoptosis and inhibition of prostaglandin-mediated angiogenesis. Compelling evidence from many observational studies has consistently documented a 40-50% redn. in the risk of adenomatous polyps, colorectal cancer incidence, and mortality in patients using NSAIDs. Recent randomized, controlled trials have demonstrated a benefit with aspirin in reducing the rate of development of new or recurrent adenomas in high-risk patients. In addn., randomized studies using sulindac and celecoxib in patients with FAP have documented significant regression of existing adenomatous polyps. CONCLUSIONS: Inhibition of COX-2 is an example of a targeted approach to the chemoprevention of colorectal cancer. However, controversy exists about the safety, efficacy, and optimal treatment regimen of NSAIDs as long-term chemopreventive agents in the general population. Ongoing studies in high-risk patients with both selective and nonselective COX inhibitors will provide important information in the area of colorectal chemoprevention, but clin. trials' use of adenomas as surrogate markers for chemoprevention trials makes their application to the general population limited.

IT **169590-42-5**, Celecoxib
RL: ADV (Adverse effect, including toxicity); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(use of NSAIDs for chemoprevention of colorectal **cancer**)

RN 169590-42-5 HCAPLUS

CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L19 ANSWER 2 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:855661 HCAPLUS
DOCUMENT NUMBER: 139:333103
TITLE: Method of using a cyclooxygenase-2 inhibitor and one

or more ornithine decarboxylase inhibitors as a combination therapy in the treatment of neoplasia

INVENTOR(S): Masterrer, Jaime L.
PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 857,873.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 17
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003203956	A1	20031030	US 2002-212523	20020805
WO 2000038730	A2	20000706	WO 1999-US30693	19991222
WO 2000038730	A3	20001102		

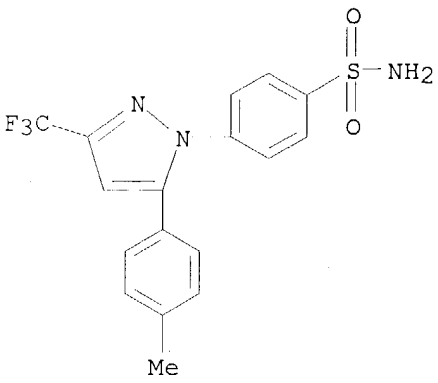
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30693 W 19991222
US 2001-857873 A2 20011005

AB A method is described for treating or preventing a neoplasia disorder in a mammal in need of such treatment or prevention, which method comprises administering to the mammal a therapeutically-effective amt. of a combination of a cyclooxygenase-2 inhibitor and one or more ornithine decarboxylase inhibitors. Mice injected with HT-20 colon carcinoma cells were treated with celecoxib.

IT **169590-42-5**, Celecoxib
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(as cyclooxygenase-2 inhibitor; cyclooxygenase-2 inhibitor and one or more ornithine decarboxylase inhibitors for combination therapy of **neoplasia**)

RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L19 ANSWER 3 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:814755 HCAPLUS
DOCUMENT NUMBER: 139:358262
TITLE: Suppression of N-methyl-N-nitrosourea/testosterone-induced rat prostate cancer growth by celecoxib: effects on cyclooxygenase-2, cell cycle regulation, and apoptosis mechanism(s)
AUTHOR(S): Narayanan, Bhagavathi A.; Condon, Mark S.; Bosland, Maarten C.; Narayanan, Narayanan K.; Reddy, Bandaru S.
CORPORATE SOURCE: Division of Nutritional Carcinogenesis, American Health Foundation, Valhalla, NY, 10595, USA
SOURCE: Clinical Cancer Research (2003), 9(9), 3503-3513
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

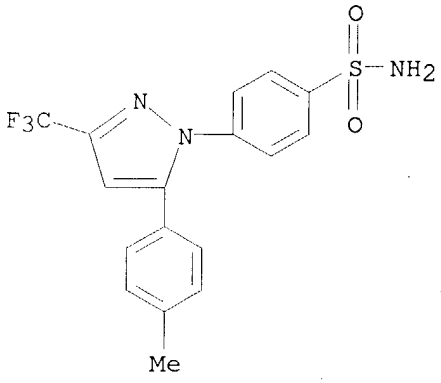
AB Purpose: This study was aimed at examg. the mechanisms underlying the chemopreventive effect of celecoxib against prostate cancer. We focused our attention on events at the cellular level to show the ability of celecoxib to inhibit prostate cancer growth, by inducing cell cycle arrest and apoptosis. Moreover, we attempted to demonstrate the expression of genes involved in the downstream events related to cyclooxygenase-2 (COX-2) regulation and apoptosis. Exptl. Design: To det. the level of COX-2 expression, we used paraffin-embedded tumor tissue sections and cancer cells (I-26) derived from N-methyl-N-nitro-so-urea/testosterone-induced rat dorsolateral prostate, and we used immunofluorescence detection and Western blot analyses with anti-COX-2 monoclonal antibodies. We conducted clonogenic cell survival assays to demonstrate cell growth inhibition at very low doses of celecoxib. Flow cytometric anal. demonstrated the effects on the cell cycle. Reverse transcription-PCR and Western blot analyses were performed to show the effect of celecoxib on the downstream events of COX-2 and apoptosis-related targets. Results: The summary of our findings indicates that (a) these cells from chem. induced rat prostate tumors express COX-2 at both the mRNA and the protein level; (b) celecoxib significantly reduces COX-2 expression in these cancer cells; and (c) celecoxib induces cell cycle arrest at the G1-S phase transition point and modifies cell cycle regulatory proteins such as cyclin D1, retinoblastoma (Rb), and phosphorylated Rb, cyclin E, p27KIP1, and p21WAF1/CIP1. Furthermore, celecoxib inhibits DNA synthesis and induces apoptosis. Most importantly, celecoxib-induced apoptosis was assocd. with down-regulation of COX-2, nuclear factor .kappa.Bp65, and

with activation of peroxisome proliferator-activated receptor .gamma., apoptosis activating factor-1, and caspase-3. Conclusion: Results from the present study clearly indicate that celecoxib exerts its anticancer effect partly through COX-2-independent mechanisms in addn. to the known primary function of COX-2 inhibition.

IT **169590-42-5**, Celecoxib
RL: **DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(celecoxib suppression of prostate **cancer** growth: effects on cyclooxygenase-2, cell cycle regulation, and apoptosis)

RN 169590-42-5 HCAPLUS

CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:698397 HCAPLUS
DOCUMENT NUMBER: 139:270500
TITLE: The cyclooxygenase-2-selective inhibitors rofecoxib and celecoxib prevent colorectal neoplasia occurrence and recurrence
AUTHOR(S): Rahme, Elham; Barkun, Alan N.; Toubouti, Youssef; Bardou, Marc
CORPORATE SOURCE: Department of Medicine, McGill University, Montreal, Can.
SOURCE: Gastroenterology (2003), 125(2), 404-412
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

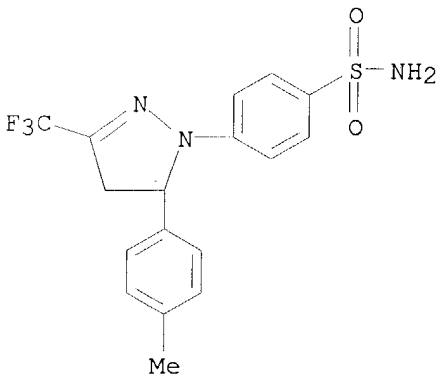
AB Colorectal cancer is one of the leading causes of cancer death. Most colorectal cancers are believed to develop from colorectal adenomas. We examd. the effect of the selective cyclooxygenase-2 inhibitors rofecoxib and celecoxib, nonselective nonsteroidal anti-inflammatory drugs, aspirin, and acetaminophen on colorectal neoplasia (colorectal cancer, colorectal adenoma, or both). This was a nested case-control study, which used data from a government insurance database on patients 65 yr and older who underwent a diagnostic test or procedure for colorectal neoplasia between

Jan. and June 2001. Logistic regression models were used to det. the effect of exposure to the drugs of interest for at least 3 mo on the occurrence or recurrence of colorectal neoplasia. The control group included 2568 patients found to be free of colorectal neoplasia; 730 patients were diagnosed with colorectal adenoma, and 179 were diagnosed with colorectal cancer. Patients more likely to have colorectal adenoma (odds ratio, 95% confidence interval) were those diagnosed with colorectal adenoma (4.12, 3.27-5.18) or colorectal cancer (3.74, 2.32-6.03) in the previous 1-3 yr and those with hemorrhage of the rectum or unspecified anemia in the prior month (3.19, 2.46-4.12). Exposures to rofecoxib (0.67, 0.46-0.98) and nonselective nonsteroidal anti-inflammatory drugs (0.41, 0.21-0.83) reduced the risk of colorectal adenoma. Rofecoxib, celecoxib, and nonselective nonsteroidal anti-inflammatory drugs were all protective against both neoplasias (0.64, 0.45-0.91; 0.73, 0.54-0.99; and 0.47, 0.26-0.86, resp.). Rofecoxib, celecoxib, and nonselective nonsteroidal antiinflammatory drugs seem to protect against the development of colorectal neoplasia.

IT **169590-42-5**, Celecoxib
RL: **PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2-selective inhibitors rofecoxib and celecoxib and nonspecific NSAIDs prevent colorectal **neoplasia** occurrence and recurrence)

RN 169590-42-5 HCAPLUS

CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

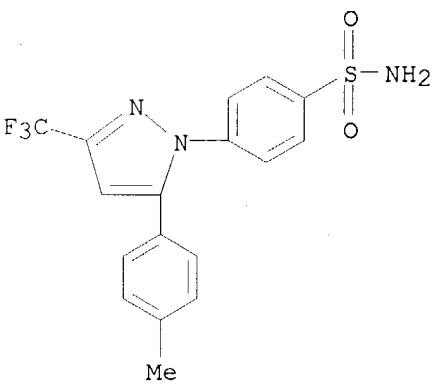
L19 ANSWER 5 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:683098 HCAPLUS
DOCUMENT NUMBER: 139:270493
TITLE: The 15-lipoxygenase-1 product 13-S-hydroxyoctadecadienoic acid down-regulates PPAR-.delta. to induce apoptosis in colorectal cancer cells
AUTHOR(S): Shureiqi, Imad; Jiang, Wei; Zuo, Xiangsheng; Wu, Yuanqing; Stimmel, Julie B.; Leesnitzer, Lisa M.; Morris, Jeffrey S.; Fan, Hui-Zhen; Fischer, Susan M.; Lippman, Scott M.

CORPORATE SOURCE: Department of Clinical Cancer Prevention, University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(17), 9968-9973
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Diminished apoptosis, a crit. event in tumorigenesis, is linked to down-regulated 15-lipoxygenase-1 (15-LOX-1) expression in colorectal cancer cells. 13-S-hydroxyoctadecadienoic acid (13-S-HODE), which is the primary product of 15-LOX-1 metab. of linoleic acid, restores apoptosis. Nonsteroidal antiinflammatory drugs (NSAIDs) transcriptionally up-regulate 15-LOX-1 expression to induce apoptosis. Peroxisome proliferator-activated receptors (PPARs) are nuclear receptors for linoleic and arachidonic acid metabolites. PPAR-.delta. promotes colonic tumorigenesis. NSAIDs suppress PPAR-.delta. activity in colon cancer cells. The mechanistic relationship between 15-LOX-1 and PPAR-.delta. was previously unknown. Our current study shows that. (i) 13-S-HODE binds to PPAR-.delta., decreases PPAR-.delta. activation, and down-regulates PPAR-.delta. expression in colorectal cancer cells;. (ii) the induction of 15-LOX-1 expression is a crit. step in NSAID down-regulation of PPAR-.delta. and the resultant induction of apoptosis; and. (iii) PPAR-.delta. is an important signaling receptor for 13-S-HODE-induced apoptosis. The in vivo relevance of these mechanistic findings was demonstrated in our tumorigenesis studies in nude mouse xenograft models. Our findings indicate that the down-regulation of PPAR-.delta. by 15-LOX-1 through 13-S-HODE is an apoptotic signaling pathway that is activated by NSAIDs.

IT **169590-42-5**, Celecoxib
RL: **DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(downregulation of PPAR-.delta. by 15-lipoxygenase-1 through 13-S-hydroxyoctadecadienoic acid is an apoptotic signaling pathway that is activated by NSAIDs in colorectal **cancer** cells)

RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 67 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:456927 HCAPLUS
DOCUMENT NUMBER: 133:84243
TITLE: Method of using a cyclooxygenase-2 inhibitor and one or more antineoplastic agents as a combination therapy in the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 236 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 17
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038730	A2	20000706	WO 1999-US30693	19991222
WO 2000038730	A3	20001102		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356606	AA	20000706	CA 1999-2356606	19991222
EP 1140192	A2	20011010	EP 1999-967543	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9916518	A	20020129	BR 1999-16518	19991222
JP 2002533416	T2	20021008	JP 2000-590681	19991222
ZA 2001005055	A	20020920	ZA 2001-5055	20010620
ZA 2001005120	A	20020107	ZA 2001-5120	20010621
NO 2001003155	A	20010822	NO 2001-3155	20010622
US 2003119895	A1	20030626	US 2002-150546	20020516
US 2003203956	A1	20031030	US 2002-212523	20020805

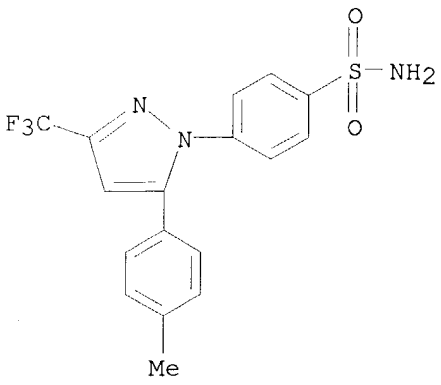
PRIORITY APPLN. INFO.: US 1998-113786P P 19981223
WO 1999-US30693 W 19991222
US 2001-857873 A2 20011005

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a cyclooxygenase-2 inhibitor and an antineoplastic agent.

IT **169590-42-5**, Celecoxib
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor-**antineoplastic** agent combination for **neoplasia** treatment)

RN 169590-42-5 HCAPLUS

CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



L19 ANSWER 68 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:456913 HCAPLUS
DOCUMENT NUMBER: 133:84241
TITLE: Combination therapy of radiation and a cyclooxygenase 2 (COX-2) inhibitor for the treatment of neoplasia
INVENTOR(S): McKearn, John P.; Masferrer, Jaime L.; Milas, Luka
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 17
PATENT INFORMATION:

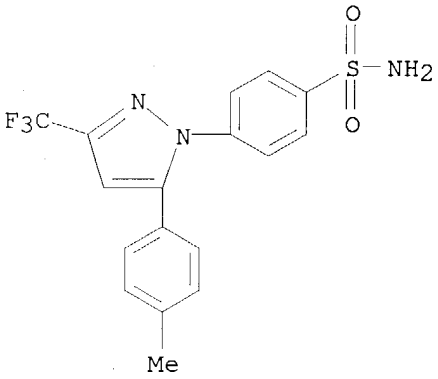
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038716	A1	20000706	WO 1999-US30669	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6649645	B1	20031118	US 1999-385214	19990827
CA 2356547	AA	20000706	CA 1999-2356547	19991222
EP 1140181	A1	20011010	EP 1999-968939	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9916544	A	20020108	BR 1999-16544	19991222
JP 2002535249	T2	20021022	JP 2000-590667	19991222
NO 2001003064	A	20010823	NO 2001-3064	20010620

PRIORITY APPLN. INFO.:
US 1998-113786P P 19981223
US 1999-385214 A 19990827
WO 1999-US30669 W 19991222

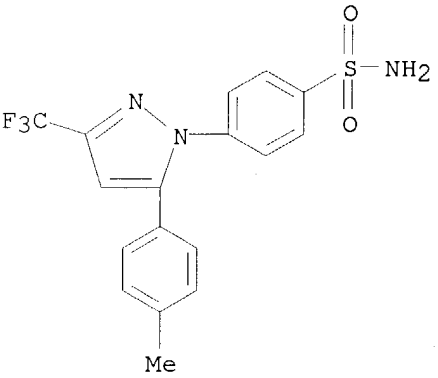
AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of radiation therapy and a COX-2 inhibitor.

IT **169590-42-5 169590-42-5D**, derivs.
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(COX-2 inhibitor-radiotherapy combination for **neoplasia** treatment)

RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 69 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:441655 HCAPLUS
DOCUMENT NUMBER: 133:68922
TITLE: Method of using a cyclooxygenase-2 inhibitor and a matrix metalloproteinase inhibitor as a combination therapy in the treatment of neoplasia

INVENTOR(S): McKearn, John P.; Gordon, Gary; Cunningham, James J.; Gately, Stephen T.; Koki, Alane T.; Masferrer, Jaime L.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA
SOURCE: PCT Int. Appl., 437 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 17
PATENT INFORMATION:

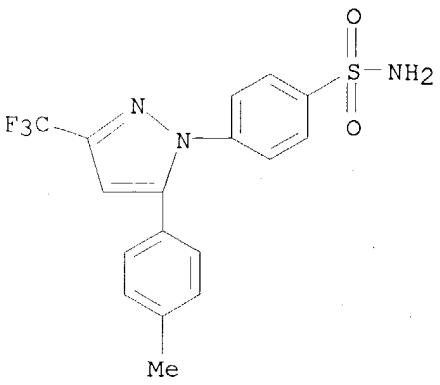
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037107	A2	20000629	WO 1999-US30776	19991222
WO 2000037107	A3	20010201		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356426	AA	20000629	CA 1999-2356426	19991222
EP 1140194	A2	20011010	EP 1999-968540	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9916536	A	20020102	BR 1999-16536	19991222
JP 2002532563	T2	20021002	JP 2000-589217	19991222
ZA 2001005055	A	20020920	ZA 2001-5055	20010620
ZA 2001005120	A	20020107	ZA 2001-5120	20010621
NO 2001003156	A	20010823	NO 2001-3156	20010622
PRIORITY APPLN. INFO.:			US 1998-113786P P	19981223
			WO 1999-US30776 W	19991222

AB Methods are provided to treat or prevent neoplasia disorders in a mammal using a combination of a cyclooxygenase-2 inhibitor, a matrix metalloproteinase inhibitor and an antineoplastic agent.

IT **169590-42-5**, Celecoxib
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor and matrix metalloproteinase inhibitor in combination therapy for **neoplasia** treatment)

RN 169590-42-5 HCAPLUS

CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

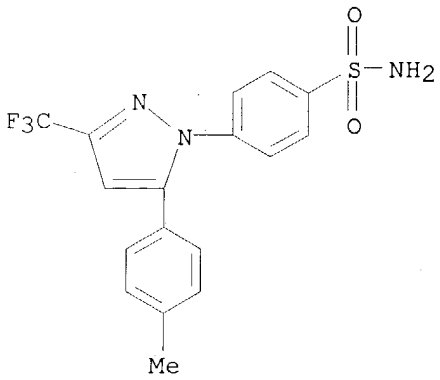


L19 ANSWER 70 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:282718 HCAPLUS
DOCUMENT NUMBER: 133:53326
TITLE: Chemoprevention of breast cancer in rats by celecoxib, a cyclooxygenase 2 inhibitor
AUTHOR(S): Harris, Randall E.; Alshafie, Galal A.; Abou-Issa, Hussein; Seibert, Karen
CORPORATE SOURCE: School of Public Health, Comprehensive Cancer Center, The Ohio State University College of Medicine, Columbus, OH, 43210, USA
SOURCE: Cancer Research (2000), 60(8), 2101-2103
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nonsteroidal anti-inflammatory drugs (NSAIDs) have been obsd. to reduce the relative risk of breast cancer. This prompted our investigation of the chemopreventive potential of celecoxib, a specific cyclooxygenase 2 blocker, against mammary carcinogenesis induced by 7,12-dimethylbenz(a)anthracene in female Sprague Dawley rats. Treatment with celecoxib was examd. and compared to treatment with the general NSAID, ibuprofen, and to a control group receiving only dimethylbenz(a)anthracene. Dietary administration of celecoxib (1500 ppm) produced striking redns. in the incidence, multiplicity, and vol. of breast tumors relative to the control group (68%, 86%, and 81%, resp.; $P < 0.001$). Ibuprofen also produced significant effects, but of lesser magnitude (40%, 52%, and 57%, resp.; $P < 0.001$). These results help confirm the chemopreventive activity of NSAIDs against breast cancer and provide the first evidence that a cyclooxygenase 2 blocking agent, celecoxib, possesses strong chemopreventive activity against mammary carcinogenesis.

IT **169590-42-5**, Celecoxib
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(chemoprevention of breast **cancer** in rats by celecoxib, a cyclooxygenase 2 inhibitor)

RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

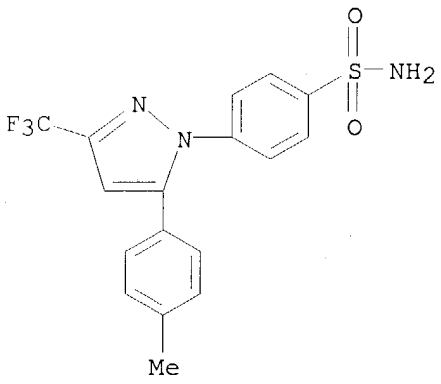
L19 ANSWER 71 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:270293 HCAPLUS
DOCUMENT NUMBER: 133:37879
TITLE: The cyclooxygenase-2 inhibitor celecoxib induces apoptosis by blocking Akt activation in human prostate cancer cells independently of Bcl-2
AUTHOR(S): Hsu, Ao-Lin; Ching, Tsui-Ting; Wang, Da-Sheng; Song, Xueqin; Rangnekar, Vivek M.; Chen, Ching-Shih
CORPORATE SOURCE: Division of Pharmaceutical Sciences, College of Pharmacy, University of Kentucky, Lexington, KY, 40536, USA
SOURCE: Journal of Biological Chemistry (2000), 275(15), 11397-11403
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study investigates the apoptotic activity of the cyclooxygenase-2 (COX-2) inhibitor celecoxib in prostate carcinoma cells. COX-2 is constitutively expressed in androgen-responsive LNCaP and androgen-nonresponsive PC-3 cells. Exposure of these cells to celecoxib induces characteristic features of apoptosis, including morphol. changes, DNA laddering, and caspase-3 activation, whereas piroxicam, a COX-1-specific inhibitor, displays no appreciable effect on either cancer cell line even after prolonged exposure. Moreover, the potency of celecoxib in apoptosis induction is significantly higher than that of other COX-2 inhibitors examd. despite the observation that these inhibitors exhibit similar IC50 in COX-2 inhibition. It is noteworthy that normal human prostate epithelial cells, expressing a marginally detectable level of COX-2, are insensitive to the induction of apoptosis by celecoxib. These data suggest a correlation between COX-2 expression and sensitivity to the apoptotic effect of the COX-2 inhibitor. In an effort to delineate the underlying mechanism, we examd. the effect of celecoxib on the expression of Bcl-2 as well as the activation of the key anti-apoptotic kinase Akt. In contrast to an earlier report that attributed the apoptotic activity of NS398 in LNCaP cells to Bcl-2 down-regulation, we provide evidence that the induction of apoptosis by

celecoxib in LNCaP and PC-3 cells is independent of Bcl-2. First, treatment with celecoxib does not alter the cellular Bcl-2 level in both cell lines. Second, enforced Bcl-2 expression in PC-3 cells does not confer protection against the induction of apoptosis by celecoxib. Our data show that celecoxib treatment blocks the phosphorylation of Akt. This correlation is supported by studies showing that overexpression of constitutively active Akt protects PC-3 cells from celecoxib-induced apoptosis. Nevertheless, how celecoxib down-regulates Akt is not clear because the drug does not adversely affect phosphoinositide 3-kinase activity in vivo and okadaic acid, a protein phosphatase 2A inhibitor, cannot rescue the inhibition. In summary, our data demonstrate that inhibition of Akt activation may play a crucial role in the induction of apoptosis by celecoxib.

IT **169590-42-5**, Celecoxib
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitor celecoxib induces apoptosis by blocking Akt activation in human prostate **cancer** cells independently of Bcl-2)

RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 72 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:191850 HCAPLUS
DOCUMENT NUMBER: 132:329541
TITLE: Antiangiogenic and antitumor activities of cyclooxygenase-2 inhibitors
AUTHOR(S): Masferrer, Jaime L.; Leahy, Kathleen M.; Koki, Alane T.; Zweifel, Ben S.; Settle, Steven L.; Woerner, B. Mark; Edwards, Dorothy A.; Flickinger, Amy G.; Moore, Rosalyn J.; Seibert, Karen
CORPORATE SOURCE: G. D. Searle/Monsanto Company, St. Louis, MO, 63167, USA
SOURCE: Cancer Research (2000), 60(5), 1306-1311
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office

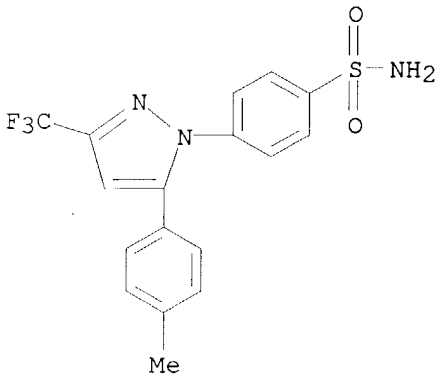
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We provide evidence that cyclooxygenase (COX)-2-derived prostaglandins contribute to tumor growth by inducing newly formed blood vessels (neoangiogenesis) that sustain tumor cell viability and growth. COX-2 is expressed within human tumor neovasculature as well as in neoplastic cells present in human colon, breast, prostate, and lung cancer biopsy tissue. COX-1 is broadly distributed in normal, as well as in neoplastic, tissues. The contribution of COX-2 to human tumor growth was indicated by the ability of celecoxib, an agent that inhibits the COX-2 enzyme, to suppress growth of lung and colon tumors implanted into recipient mice. Mechanistically, celecoxib demonstrated a potent antiangiogenic activity. In a rat model of angiogenesis, we observe that corneal blood vessel formation is suppressed by celecoxib, but not by a COX-1 inhibitor. These and other data indicate that COX-2 and COX-2-derived prostaglandins may play a major role in development of cancer through numerous biochem. mechanisms, including stimulation of tumor cell growth and neovascularization. The ability of celecoxib to block angiogenesis and suppress tumor growth suggests a novel application of this anti-inflammatory drug in the treatment of human cancer.

IT **169590-42-5**, Celecoxib
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antiangiogenic and **antitumor** activities of cyclooxygenase-2 inhibitors)

RN 169590-42-5 HCAPLUS

CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 73 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:102215 HCAPLUS
DOCUMENT NUMBER: 132:260309
TITLE: Chemoprevention of colon cancer by specific cyclooxygenase-2 inhibitor, celecoxib, administered during different stages of carcinogenesis
AUTHOR(S): Reddy, Bandaru S.; Hirose, Yoshinobu; Lubet, Ronald; Steele, Vernon; Kelloff, Gary; Paulson, Susan;

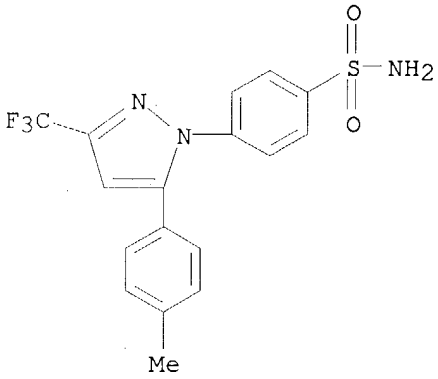
Seibert, Karen; Rao, Chinthalapally V.
CORPORATE SOURCE: Division of Nutritional Carcinogenesis and Chemoprevention Program, American Health Foundation, Valhalla, NY, 10595, USA
SOURCE: Cancer Research (2000), 60(2), 293-297
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Epidemiol. observations and lab. research have suggested that nonsteroidal anti-inflammatory drugs (NSAIDs) reduce the risk of colon cancer and that the inhibition of colon carcinogenesis by NSAIDs is mediated through the modulation of prostaglandin prodn. by rate-limiting enzymes known as cyclooxygenases (COXs). Because traditional NSAIDs inhibit both COX-1 and COX-2, these drugs induce side effects, such as gastrointestinal ulceration and renal toxicity, through the inhibition of the constitutive COX-1. Overexpression of COX-2 has been obsd. in colon tumors; therefore, specific inhibitors of COX-2 could serve as chemopreventive agents. Our previous study has shown that celecoxib, an inhibitor of COX-2, while sparing COX-1, inhibited azoxymethane (AOM)-induced colon tumorigenesis when administered during both initiation and postinitiation stages, i.e., celecoxib administered continuously before, during, and after carcinogen treatment. This study examd. the dose-response effect of celecoxib when administered during the initiation and postinitiation stages. In addn., the chemopreventive effects of high-dose celecoxib administered during the promotion/progression stage of colon carcinogenesis, i.e., continuous celecoxib administration beginning 14 wk after the carcinogen treatment, was detd. in male F344 rats. We also measured the steady-state levels of celecoxib in the plasma of animals given this inhibitor. Groups of 5-wk-old male F344 rats were fed either a control diet or exptl. diets contg. 500, 1000, or 1500 ppm celecoxib. At 7 and 8 wk of age, rats scheduled for carcinogen treatment were injected s.c. with AOM at a dose rate of 15 mg/kg body wt./wk. Groups of animals destined for the promotion/progression study and initially receiving the control diet were switched to a diet contg. 1500 ppm celecoxib beginning 14 wk after the second AOM treatment. All rats remained on their resp. dietary regimens until the termination of the study, i.e., 52 wk, and were then sacrificed. Colon tumors were evaluated histopathol. Administration of 500, 1000, or 1500 ppm celecoxib during the initiation and postinitiation stages significantly inhibited the incidence ($P < 0.01$ to $P < 0.0001$) as well as the multiplicity ($P < 0.01$ to $P < 0.0001$) of adenocarcinomas of the colon in a dose-dependent manner. Importantly, administration of 1500 ppm celecoxib during the promotion/progression stage also significantly suppressed the incidence and multiplicity of adenocarcinomas of the colon ($P < 0.01$). Also, administration of celecoxib to the rats during the initiation and postinitiation periods and throughout the promotion/progression stage strongly suppressed colon tumor vol. ($P < 0.0002$ to $P < 0.001$). The steady-state plasma concn. of celecoxib increases somewhat with the dose. Thus, in this model system, the chemopreventive efficacy of celecoxib is dose-dependent when this COX-2 inhibitor is administered during the initiation and postinitiation periods. This study provides the first evidence that celecoxib is also very effective when it is given during the promotion/progression stage of colon carcinogenesis, indicating that the chemopreventive efficacy is achieved during the later stages of colon tumor development. This suggests that celecoxib may potentially be an effective chemopreventive agent for the secondary prevention of colon cancer in patients with

familial adenomatous polyposis and sporadic polyps.

IT **169590-42-5**, Celecoxib
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(chemoprevention of colon **cancer** by specific cyclooxygenase-2 inhibitor, celecoxib, administered during different stages of carcinogenesis)

RN 169590-42-5 HCAPLUS

CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 74 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:686709 HCAPLUS
DOCUMENT NUMBER: 131:307089
TITLE: Method using cyclooxygenase-2 inhibitors in the treatment and prevention of neoplasia
INVENTOR(S): Seibert, Karen; Masferrer, Jaime; Gordon, Gary B.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5972986	A	19991026	US 1997-949922	19971014
US 2001047024	A1	20011129	US 2001-862128	20010521
US 6469040	B2	20021022		
US 2003220384	A1	20031127	US 2002-226247	20020823

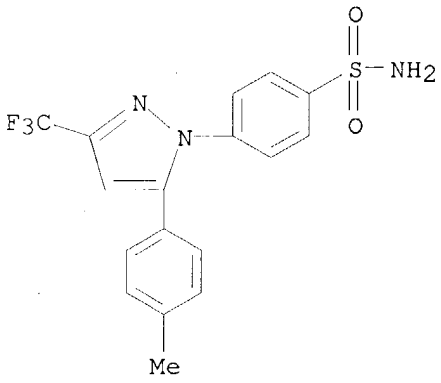
PRIORITY APPLN. INFO.: US 1997-949922 A1 19971014
US 1999-390459 B1 19990907
US 2001-862128 A3 20010521
OTHER SOURCE(S): MARPAT 131:307089

AB The invention relates to the use of cyclooxygenase-2 inhibitors or derivs. thereof in preventing and treating neoplasia. In particular, the

invention describes the method of preventing and treating epithelial cell neoplasia in a subject, said method comprising treating the subject with a therapeutically-effective amt. of I [A = (partially) unsatd. heterocyclyl, (partially) unsatd. carbocyclic ring; R1 = (substituted) heterocyclyl, (substituted) cycloalkyl, (substituted) cycloalkenyl, (substituted) aryl; R2 = Me, amino; R3 = H, halo, alkyl, alkenyl, etc.] or a pharmaceutically acceptable salt thereof.

IT **169590-42-5**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitors for treatment and prevention of **neoplasia**)

RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 75 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:675772 HCAPLUS
DOCUMENT NUMBER: 132:10407
TITLE: Reduction of UV-induced skin tumors in hairless mice by selective COX-2 inhibition
AUTHOR(S): Pentland, Alice P.; Schoggins, John W.; Scott, Glynis A.; Khan, Kanwar Nasir M.; Han, Rujing
CORPORATE SOURCE: Department of Dermatology, University of Rochester Medical Center, Rochester, NY, 14642, USA
SOURCE: Carcinogenesis (1999), 20(10), 1939-1944
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

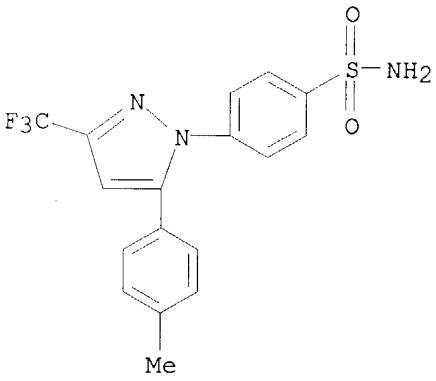
AB UV light is a complete carcinogen, inducing both basal and squamous cell skin cancers. The work described uses the selective COX-2 inhibitor celecoxib to examine the efficacy of COX-2 inhibition in the redn. of UV light-induced skin tumor formation in hairless mice. UVA-340 sun lamps were chosen as a light source that effectively mimics the solar UVA and UVB spectrum. Hairless mice were irradiated for 5 days a week for a total dose of 2.62 J/cm2. When 90% of the animals had at least one tumor, the

mice were divided into two groups so that the tumor no. and multiplicity were the same (P<0.31). Half of the mice were then fed a diet contg. 1500 p.p.m. celecoxib. Tumor no., multiplicity and size were then obsd. for the next 10 wk. Ninety-five percent of the tumors formed were histopathol. evaluated as squamous cell carcinoma. COX-2 expression and activity were increased in tumors. After 10 wk, the difference in tumor no. and multiplicity in the drug-treated group was 56% of UV controls (P<0.001). The results show that the orally administered selective COX-2 inhibitor celecoxib prevents new tumor formation after the onset of photocarcinogenesis and suggest that treatment with celecoxib may be very useful in preventing UV-induced skin tumors in humans.

IT **169590-42-5**, Celecoxib
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(COX-2 inhibition redn. of UV-induced skin **tumors**)

RN 169590-42-5 HCAPLUS

CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 76 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:440003 HCAPLUS
DOCUMENT NUMBER: 131:82985
TITLE: Use of cyclooxygenase-2 inhibitors for the treatment and prevention of tumors, tumor-related disorders and cachexia
INVENTOR(S): Kurakata, Shinichi; Hanai, Masaharu; Kanai, Saori; Kimura, Tomio
PATENT ASSIGNEE(S): Sankyo Company Limited, Japan
SOURCE: Eur. Pat. Appl., 49 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 927555	A1	19990707	EP 1998-310510	19981221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 333399	A	20000526	NZ 1998-333399	19981216
JP 11246403	A2	19990914	JP 1998-362188	19981221
ZA 9811840	A	19990623	ZA 1998-11840	19981223
NO 9806089	A	19990625	NO 1998-6089	19981223
RU 2190399	C2	20021010	RU 1998-124076	19981223
AU 9898225	A1	19990715	AU 1998-98225	19981224
AU 745865	B2	20020411		
CN 1230407	A	19991006	CN 1998-111656	19981224
BR 9805544	A	20000328	BR 1998-5544	19981224
MX 9900134	A	20000630	MX 1999-134	19990104
JP 11279078	A2	19991012	JP 1999-14059	19990122
JP 2000095685	A2	20000404	JP 1999-176139	19990623
JP 3214695	B2	20011002		
JP 2000159690	A2	20000613	JP 1999-176140	19990623

PRIORITY APPLN. INFO.:
JP 1997-354499 A 19971224
JP 1998-15306 A 19980128
JP 1998-204907 A 19980721
JP 1998-269444 A 19980924

OTHER SOURCE(S): MARPAT 131:82985

AB Certain cyclooxygenase-2 inhibitors are useful for the treatment and prevention of tumors and tumor-related disorders and cachexia.

IT **169590-42-5**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitors for treatment and prevention of **tumors, tumor**-related disorders, and cachexia)

RN 169590-42-5 HCAPLUS

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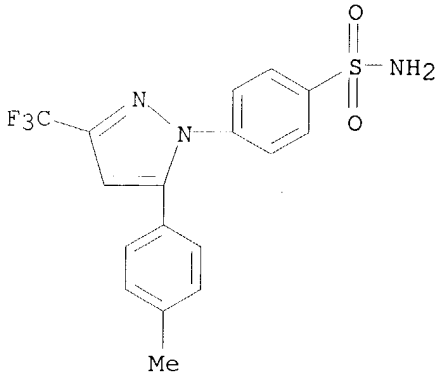

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 77 OF 77 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:251054 HCAPLUS
DOCUMENT NUMBER: 128:304042
TITLE: Method of using cyclooxygenase-2 inhibitors in the

treatment and prevention of neoplasia
INVENTOR(S): Seibert, Karen; Masferrer, Jaime; Gordon, Gary B.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA; Seibert, Karen; Masferrer, Jaime; Gordon, Gary B.
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9816227	A1	19980423	WO 1997-US18670	19971014
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2372912	AA	19980423	CA 1997-2372912	19971014
AU 9749048	A1	19980511	AU 1997-49048	19971014
AU 742645	B2	20020110		
EP 932402	A1	19990804	EP 1997-911746	19971014
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9712314	A	19990831	BR 1997-12314	19971014
JP 2001503395	T2	20010313	JP 1998-518591	19971014
NZ 334921	A	20010330	NZ 1997-334921	19971014
CA 2267186	C	20020514	CA 1997-2267186	19971014
NZ 506515	A	20020531	NZ 1997-506515	19971014
NO 9901793	A	19990415	NO 1999-1793	19990415
NZ 509755	A	20020927	NZ 2001-509755	20010207

PRIORITY APPLN. INFO.:
US 1996-28494P P 19961015
CA 1997-2267186 A3 19971014
WO 1997-US18670 W 19971014
NZ 2001-334921 A1 20010207

OTHER SOURCE(S): MARPAT 128:304042

AB Cyclooxygenase-2 inhibitors or derivs. thereof are used in preventing and treating neoplasia. In particular, the invention describes the method of preventing and treating epithelial cell neoplasia in a subject, said method comprising treating the subject with a therapeutically-effective amt. of e.g. p-(R2SO2)PhA(R1)(R3) [A = (partially) unsatd. heterocyclyl, (partially) unsatd. carbocyclyl; R1 = (substituted) heterocyclyl, (substituted) cycloalk(en)yl, (substituted) aryl; R2 = Me, amino; R3 = H, halo, alkyl, etc.].

IT **169590-42-5**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitors for treatment and prevention of **neoplasia**)

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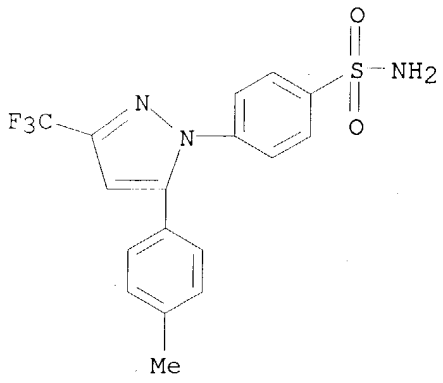

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT